Geriatric dermatology: optimising care in frail older adults

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“It's not how old you are, it's how you are old.”

Jules Renard (Frans schrijver, 1864-1910)

Contents

1

General introduction, thesis aims and outline

The aging of the world population ("global graying") creates many emergent challenges in different perspectives. Dermatologists and other providers of dermatological care are confronted with a growing number of -often frail- older adults. Frailty is defined as "a state of vulnerability to poor resolution of homoeostasis after a stressor event and is a consequence of cumulative decline in many physiological systems during a lifetime."[1] Consequently, minor stressor events can result in disproportionate health changes in frail older adults. Within this specific population skin problems are common, which may cause a high level of morbidity leading to a significant impact on quality of life.[2-4] Factors that might contribute to the development of skin disorders often should be taken into consideration in older adults (e.g. immobility, incontinence, and comorbidities). Furthermore, general factors like a limited life expectancy or cognitive impairment deserve proper attention as well during medical decision making. Caregivers frequently face challenges and dilemma's regarding these themes in daily clinical practice. In this introduction, the aging world population, skin aging and common dermatological disorders among older adults will be discussed. Special attention will be paid to skin cancer. Furthermore, an overview will be given on the organization of dermatologic care in older adults.

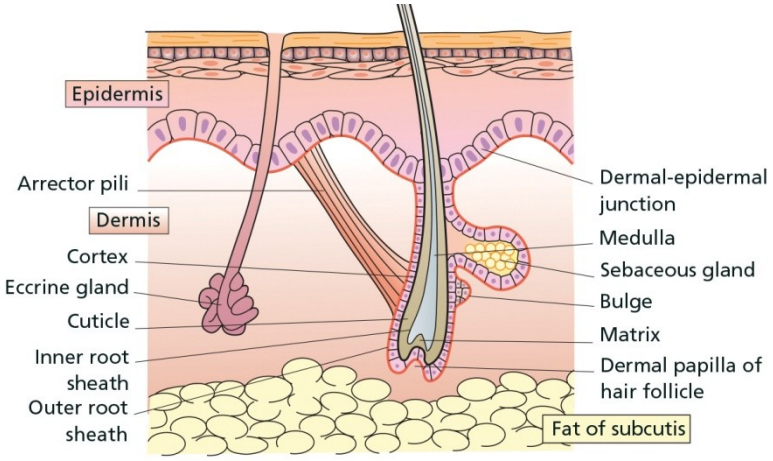
1.1 Population aging

Life expectancy increases worldwide due to factors like improving healthcare and a decline in the average number of children born per family (the latter is mainly the case in Western countries). According to calculations of the World Health Organisation the mean worldwide life expectancy (at birth) will increase by 15 years during this century, up to 83 years in 2100. In most Western countries the mean life expectancy is even expected to pass 90 years during this century. Consequently, the number of oldest-old persons in the world, defined as persons aged 80 years and over, is expected to increase rapidly from 125 million in 2015 to approximately 1 billion in 2100. The greatest proportion of oldest-old persons lives in Europe (28% of all oldest-old persons in the world lives in Europe).[5] Focusing on the Netherlands, the most recent predictions of Statistics Netherlands *(Dutch: Centraal Bureau voor de Statistiek)* state the number of persons aged 80 years and over keeps increasing to 2053. Statistics Netherlands expects the number of oldest-old will triple in the period 2014-2060, resulting in 2 million oldest-old people in the Netherlands in 2060, which is 11% of the total population. Current aging in the Netherlands seems both related to a decreasing mortality rate due to improving life style (e.g. less smoking) and medical development, as well as the currently aging baby-boom generation (the significant birth wave which was noted in the Netherlands after the Second World War between 1946-1955).[6,7]

1.2 Anatomy and functions of the skin

To be able to understand the process of skin aging it is important to provide some basics regarding the anatomy and functioning of the skin first. The human skin (*Latin: cutis*) is composed of two major layers: the epidermis (outer layer) and the dermis. The epidermis could be further subdivided in several other layers (*Latin: strata)* and residents three major cell types (keratinocytes, melanocytes and Langerhans cells), of which keratinocytes represent the most numerous population. Figure 1 provides a schematic overview of the different anatomic structures of the skin

Figure 1 Anatomy of the skin, modified from Burns et al.[10]



The main function of the epidermis is a protective barrier function (e.g. prevention of water loss and invasion of pathogens). The dermis could be subdivided into the papillary and reticular region and consists of a mucopolysaccharide gel and fibroelastic network of collagen and elastin (extracellular matrix), which provides structural support to the skin. The dermis contains different cell types (e.g. fibroblasts, macrophages, and mast cells) as well as a vascular and nerve system providing circulation, nutrition and sensatory information. Furthermore, it also contains skin appendages as sweat glands, hair follicles, and sebaceous glands. Directly beneath the skin a layer of subcutaneous tissue is found *(Latin: subcutis)*, which consists mostly of fat cells and has an important function in thermal isolation, attachment of the skin to deeper tissue layers and absorbing shocks.[8,9]

1.3 Skin aging

Various changes occur in the skin with aging, influenced by several factors. Skin aging processes and related influencing factors are often classified in intrinsic and extrinsic skin aging.[11-14] Many changes in the aging skin are influenced by both intrinsic and extrinsic factors and probably a lot of these influences and interactions are still unknown. Most of the changes in the aging skin relate (directly or indirectly) to common skin disorders in older adults, for instance a decrease in sebaceous gland function increasing the risk for xerosis and asteatotic dermatitis.[11,13,14] In the next paragraphs a summary is given regarding the most important changes related to skin aging in more detail (please note these paragraphs are not exhaustive).

1.3.1 Intrinsic skin aging

Intrinsic skin aging is a process induced by physiological skin maturation and is also called chronological skin aging. Intrinsic skin aging results in a decrease and alteration of several functions of the skin and its different components (e.g. epidermal barrier function, immune function, and wound healing).[11,13,14] An overview is given in Table 1.

Epidermal changes

With the intrinsic aging of the skin several changes occur within the epidermis. Both the number of epidermal cell layers and the turnover time of epidermal cells reduce, which for instance results in a diminished repair capacity of the skin after trauma.[11,14] In addition, a recent meta-analysis showed increasing age is a strong predictor for loosening of the dermo-epidermal adhesion as well, which further increases the risk for skin trauma (e.g. blister formation and shear-type injuries).[15] Furthermore, the endogenous emolliation of the skin diminishes with increasing age, which is thought to be a result of changes in both lipid synthesis and processing and seems closely related to changes in stratum corneum acidification.[16] These changes result in a diminished epidermal barrier function, which increases the risk for several skin disorders (e.g. xerosis, pruritus and contact dermatitis).[11,14,16]

Immunosenescence

Aging of the immune system is typically called “immunosenescence”. Both changes in the innate and in the adaptive immune system are observed.[11,14] Examples of these changes are a diminished number of antigen-presenting Langerhans cells in the epidermis and a decreasing production and function of B- and T-cells with advancing age.[17,18] Consequently, both the incidences of infections and cancer of the skin are higher among older adults.[11,14]

Wound healing

Several age-related changes in the skin and its components attribute to both an increased risk to develop skin ulcers and a delayed wound healing in the aged skin. Examples are structural changes like loss and changes in the extracellular matrix, altered vascular and inflammatory responses, a diminished fibroblast replication and changes in the sensatory function of the skin due to a decreasing amount of nerve endings within the dermis.[19]

Other changes

Various other skin changes occur with aging including, but not limited to, a reduced capacity to produce sweat, a decreased vitamin D synthesis, reduction in subcutaneous fat, and a decreased hair and nail growth.[11,13]

1.3.2 Extrinsic skin aging

Extrinsic aging is caused by environmental factors, of which exposure to ultraviolet radiation (UVR; photo-aging) is most important.[11-13,20]

Photo-aging

During a lifetime the human skin is frequently exposed to UVR, which strongly varies between persons due to factors like sun-protection behavior, the use of tanning devices, occupation, and geographical location. The skin is equipped with several protective mechanisms to reduce damage caused by UVR, which include epidermal thickening, formation and distribution of melanin pigment, DNA-repair mechanisms, and cell apoptosis. Photo-aging is defined as the skin changes caused by long-term UVR-exposure. Many of the skin changes due to intrinsic skin aging are accelerated due to photo-aging. UVR-exposure causes skin damage and photo-aging in several ways, ranging from direct DNA-alterations, to the generation of reactive oxygen specimens, stimulation of extracellular matrix breakdown, and induction of changes in signal transduction pathways, vascular structures and immunologic processes.[12,20]

Other environmental and lifestyle influences

Smoking is considered the most important exogenous skin aging factor, after UVR-exposure. Smoking accelerates several skin aging processes, e.g. the decrease of dermal collagen and elastin integrity, and microvascular changes. Also, smoking is an important risk factor for the development of squamous cell carcinoma (also discussed in section 1.5.2 "Squamous cell carcinoma").[21] Other factors potentially influencing extrinsic skin aging are air pollution and arsenic exposure.[22,23]

Table 1 An overview of the most important intrinsic skin changes with aging and their (potential) effects,[a] modified from Chang et al.[11] and Jafferany et al.[13]

Functions	Changes
Epidermal barrier function	Loss of acidification of skin surface leading to decreased function of pH-dependent enzymes; results in decreased production of skin lipids and increased corneocyte retention
	Reduced aquaporin-3 gene expression, leading to decreased skin hydration
	Slower return to barrier homeostasis after perturbation (e.g. chemical irritant)
Immune function	Decreased numbers of antigen-presenting Langerhans cells on histology
	Cell-mediated immunity altered, including shift in balance of TH1 and TH2 cells to favor TH2 predominance
Skin integrity and wound healing	Fibroblasts have increased doubling time
	Older fibroblasts have fewer remaining replicative cycles
	Altered levels of matrix metalloproteinases
	Fragmentation of extracellular matrix
	Flattening of dermal papillae, e.g. leading to an increased risk on skin injuries
	Vascular response to pressure abnormal in older skin, e.g. leading to an increased risk to develop pressure ulcers
	Decreased amount of nerve endings within the dermis, e.g. leading to an increased tendency on injuries and pressure ulcers
DNA repair mechanisms	Increased photocarcinogenesis / skin cancer risk
Vitamin D production	Decreased production, with previtamin D3 levels 2 to 3 times lower in older adults compared to younger populations
Lipogenesis	Decreased volume of subcutaneous fat, e.g. leading to an increased risk of hypothermia and less natural insulation
Sweat production	Reduced sweat production per sweat gland, e.g. leading to an increased risk of overheating and a reduced body odor

[a] *Table is not exhaustive.*

1.4 Common skin disorders in older adults

As discussed before several alterations in the aging skin increase skin vulnerability and the chance to develop a skin disorder. The most common skin disorders in both community-dwelling as institutionalized older adults are summarized in Table 2 and briefly discussed in more detail.

Table 2 Prevalences of the most common skin disorders in frail older adults

Disorders	Prevalence, median (range)[a]	References
Benign tumors	44% (1-99%)	24-29
Xerosis	30% (5-95%)	24-28,30
Fungal infections	17% (0-77%)	24-29
Premalignant tumors	14% (0-74%)	24-28
Dermatitis	9% (0-32%)	24-29
Chronic ulcers (including pressure ulcers)	4% (1-10%)	24-29,31
Malignant tumors	3% (0-13%)	24-28,32
Other infections and infestations	1% (0-23%)	24-29

[a] *Mentioned prevalences are strongly dependent on several variables, e.g. clinical setting and definitions used.*

In addition, frailty-related factors like comorbidities (e.g. thyroid disease, renal insufficiency, and diabetes mellitus), polypharmacy, immobility (e.g. leading to chronic pressure on some parts of the skin), and incontinence, often contribute to the development of skin disorders in the population of older adults as well. Examples are shown in Table 3.

1.4.1 Skin tumors

Various tumors could be present in the skin and incidence rates of most skin tumors rise with increasing age. Skin tumors may be benign, premalignant or malignant. Examples of common benign skin tumors are seborroic warts and cherry angioma.[13] Treatment of benign skin tumors could be considered in case of complaints. Premalignant and malignant skin tumors are also very common among older adults and are discussed in more detail in section 1.5 (“Skin cancer and precursors”).

Table 3 Frailty-related factors and examples of (potential) skin-related consequences

Factors	Examples of (potential) skin-related consequences
Comorbidities	Diabetes causing an increased risk for fungal infections, chronic ulcers, and pruritus[30,33-35]
	Hypothyreoidism might result in a delayed wound healing, edema, xerosis, or nail- and hair changes[11,35]
	Chronic renal disease increasing the risk for pruritus and calciphylaxis[34,35]
Polypharmacy	Increasing the risk to develop drug-induced skin conditions like maculopapular drug eruptions, acute generalized exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS)[36]
	Various medications could directly cause or attribute to the development of pruritus (e.g. calcium channel blockers, thiazides or opioids), by various mechanisms[34,37]
Immobility	Increases the risk to develop pressure ulcers[11,19,38]
	Venous hypertension and related skin conditions (including venous leg ulcers) are more common in patients with a limited mobility[39]
Incontinence	Increasing the risk for contact dermatitis (incontinence-associated dermatitis) and the development of pressure ulcers[38,40]
Malnutrition	A poor nutritional status increases the risk to develop pressure ulcers[11,19,38]
	Zinc deficiency might lead to several cutaneous manifestations, e.g. alopecia or peri-orifical dermatitis[35]

1.4.2 Xerosis and dermatitis

As discussed in section 1.3.1 ("Intrinsic skin aging") the aging skin becomes more prone to develop dryness (xerosis), which could ultimately result in asteatotic dermatitis. This is a form of dermatitis which is common among older adults and consists of itchy, red, scaling patches, mostly on the limbs. Frequent usage of water and soap increases the risk for xerosis and asteatotic dermatitis. Treatment consists of the regular application of moisturizers, diminishing the usage of water and soap, and in case of dermatitis a topical corticosteroid may be prescribed. Other forms of dermatitis (also called eczema) frequently diagnosed in older adults include (late-onset) atopic dermatitis, seborroic dermatitis, hypostatic dermatitis, (allergic or irritant) contact dermatitis, and nummular dermatitis.[13,14]

1.4.3 Chronic ulcers

Chronic ulcers are common and incidence rates rise with increasing age. Several types of chronic ulcers can be distinguished, including pressure ulcers (decubitus), venous and arterial leg ulcers, diabetic ulcers etc. Two main types of ulcers among older adult patients often seen in dermatological practice, will be discussed below: pressure ulcers and venous leg ulcers.

Pressure ulcers typically develop in areas with bony prominences exposed to chronic pressure. Important risk factors to develop pressure ulcers include immobility, loss of sensory functions in the skin, several comorbidities and a poor nutritional status (also described in section 1.3.1 "Intrinsic skin aging" and Table 3). Treatment mainly consists of avoidance of chronic pressure, while at the same time local wound/skin conditions, mobility, and nutritional status should be optimized. Surgical therapy may be necessary in some cases. Paramedics like a physical therapist, an ergotherapist, and/or a dietitian are included in a multidisciplinary treatment team on a regular basis.[13,38]

Venous leg ulcers develop in the context of chronic venous disease, which is very common in older adults. Conservative management includes compression therapy and optimizing local wound/skin conditions. Ablative and surgical therapies of varicose veins or wound closure using surgical grafts could be an option in some cases.[39]

1.4.4 Skin infections and infestations

Several skin infections are very prevalent among older adults. Fungal infections of skin and nails are most common, but bacterial (e.g. cellulitis), viral (e.g. herpes zoster), and parasitic infections are often seen as well. Older adults are thought to be especially prone to develop several skin infections due to immunosenescense (also described in section 1.3.1 "Intrinsic skin aging"), but also due to concomitant diseases like diabetes mellitus. Some common examples of skin infections and infestations are discussed below.

Fungal infections represent the most common infections of skin and nails among older adult patients. Diagnosis is usually easily made during clinical examination and established by a potassium hydroxide preparation or culture. Treatment includes several topical and systemic antifungal agents, dependent on factors like the infection site, severity, and species causing the infection.[13]

Herpes zoster, caused by re-activation of the varicella-zoster virus (which also causes chicken pox after primary infection), is regularly seen among older adult patients. A burning or stinging feeling of the skin and mild to more severe systemic complaints (fever, chills)

often precede the development of a vesicular erythematous eruption with a dermatomal distribution and local lymph node swelling. This skin condition is usually self-limiting within a few weeks, although in a significant number of patients (especially older adult patients) post-herpetic neuralgia persists, which may result in a significant impact on quality of life. Treatment is therefore often recommended in an early stage using systemic antiviral therapy combined with pain medication and local protective and drying agents like zinc oxide ointment.[13]

Scabies, which is an infestational skin disease, is frequently seen as well, especially in nursing home populations. Scabies is an infestation of the skin by the human itch mite (Sarcoptes scabiei var. hominis) and a typical clinical presentation includes severe itch and erythematous and scaling burrows, papules and papulovesicles on the wrists, interdigital spaces, buttocks, and genitalia. Scabies could spread from person to person after close and prolonged contact, which explains why outbreaks are seen in nursing homes on a regular basis.[13]

1.5 Skin cancer and precursors

Skin cancer and precursor lesions are very common among older adults, especially among the fair tanned. Skin cancer is the most common malignancy among Caucasians and its incidence is rising worldwide.[41-46] Skin cancer is most often classified in two groups: melanoma skin cancer and nonmelanoma skin cancer (NMSC). NMSC includes cutaneous squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Precursor lesions are known for both melanoma and SCC, but not for BCC. Focusing on skin cancer numbers in the Netherlands over the period 1989-2005, BCC is the most common type of skin cancer (71%), followed by SCC (16%) and melanoma (11%).[47] In addition, more rare types of skin cancer are sometimes included within the group of NMSC (constituting <2% of all skin malignancies; sometimes also called "orphan skin cancer"), e.g. cutaneous lymphomas, Merkel cell carcinoma, and various appendageal and soft tissue neoplasms.[47]

In the following paragraphs the three main types of skin cancer and their precursors will be discussed in more detail.

1.5.1 Basal cell carcinoma (BCC)

As mentioned before, BCC is the most common type of skin cancer.[48] In the Netherlands, age-standardized incidence rates increased fourfold in the period 1973-2009 (up to 165 and 157 per 100 000 person-years in 2009, for men and woman respectively). Therefore it is

currently estimated one out of five to six Dutch inhabitants will develop a BCC during their life. It should be noted incidence rates are believed to be even higher in daily practice, due to several mainly administrative reasons (e.g. most registries solely register the first BCC in a patient, although subsequent BCCs are very common).[46]

Typically, a BCC is a slowly growing tumor with a relatively low-malignant potential in which metastases are very rare. However, local tissue destruction may be significant. It is believed that BCCs arise from stem cells within the hair bulb and/or infundibulum.[49] In most BCCs a dysregulation of the "Hedgehog signaling pathway" is found, mostly due to mutations in PTCH1 or SMO, resulting in a dysregulation of cell growth and differentiation.[50]

The most important risk factor to develop this tumor is UVR-exposure (especially childhood sunburn and both intermittent recreational and occupational sun exposure). Additional risk factors are: increasing age, male sex, previous skin cancer, a fair skin type (Fitzpatrick skin type I and II), genetic predisposition (e.g. basal cell nevus syndrome), immunosuppression, arsenic exposure, previous actinic keratosis and previous PUVA or radiation therapy.[49,51,52]

Several subtypes can be distinguished and multiple classification systems are used in literature. One classification system, which is also used in the Dutch guideline for BCC, distinguishes four histopathological subtypes of BCC: (1) nodular, (2) superficial, (3) infiltrative, and (4) micronodular.[53] It should be mentioned that a significant proportion (20-74%) of BCC is reported to consist of multiple subtypes (mixed-type BCC).[54-56] Most BCCs, especially nodular BCC (nBCC), are located in the head and neck area. However, the proportion of superficial BCC (sBCC; often located on the trunk) has been increasing during the last decades, probably due to changing sun exposure habits.[53]

Various clinical features can be seen depending on the subtype, ranging from a pink or skin-colored nodule with a pearly appearance and telangiectatic vessles in nBCC, to a scaling red plaque in sBCC. In case of doubt dermoscopy could be very useful in diagnosing BCC. Dermoscopy (or epiluminoscopy) is a form of hand-held skin surface microscopy, typically including a 10-14 times magnification lens and lightning system. A punch biopsy is often performed prior to treatment to confirm the diagnosis and to determine the histopathological subtype(s). Examples are shown in Figure 2.

Several prognostic tumor-related factors are used to classify BCCs into high- and low-risk tumors. These factors are mainly based on the risk for recurrence after treatment and should be included in patient counseling and management decisions. High-risk factors known from literature include: aggressive histopathological subtype (infiltrative and/or

micronodular subtype), tumor localization within the face (especially the H-zone), tumor size, poorly defined lesions, recurrent tumors, perineural and/or vascular involvement.[49,51,53]

Figure 2 Examples of basal cell carcinoma (from left to right: nodular, superficial, and infiltrative basal cell carcinoma)

General treatment options for BCC comprise surgical excision (e.g. conventional excision or Mohs micrographic surgery), radiotherapy and local destructive therapies (e.g. cryotherapy, curettage with electrodesiccation, or laser therapy). In addition, sBCC can be treated topically by 5-fluorouracil cream or imiquimod cream, or by photodynamic therapy (using a topical photosensitizing cream, followed by illumination after a couple of hours incubation time).[49,51,53] In locally advanced or metastatic BCC which cannot be treated by the earlier mentioned treatment modalities, systemic therapy by vismodegib and sonidegib may be an option.[50]

Conflicting evidence can be found in current literature regarding the effect of various UVR-protective measurements and prevention programs on the risk for development of subsequent (pre)malignant skin lesions. Nevertheless, protection against more skin damage induced by UVR-exposure is currently considered the most important preventive strategy by many experts.[49,57] Sun protection includes the frequent and sufficient application of sunscreens, wearing sunprotective clothing (e.g. hats), and the discouragement of sun bathing and the usage of tanning devices. Follow-up examinations are scheduled based on several patient- and tumor characteristics (e.g. high or low-risk tumor, previous skin cancers,

and the ability to perform self-examinations). Usually, only patients who have had a high-risk BCC or multiple BCCs are scheduled for follow-up.

1.5.2 Cutaneous squamous cell carcinoma (SCC) and precursors

SCC is the second most common form of skin cancer (after BCC) in most Caucasian populations.[48] Actinic keratosis (AK) and Bowen's disease (BD) are precursor lesions of SCC.

Actinic keratosis (AK)

AK is extremely common, especially in the fair-skinned, but population-based research is relatively scarce. Prevalence data from a prospective population-based cohort study in the Rotterdam area showed AK could be found after total-body examination in the majority of older adults (≥70 years).[58] High strongly age-related prevalence rates were also found by other studies in Western countries.[59,60] AK (or solar keratosis) is a premalignant skin lesion, which is histopathologically characterized by intraepidermal atypical keratinocytes. Not surprisingly, risk factors for AK are highly comparable with the risk factors for BD and SCC (discussed in section 1.5.2 "Cutaneous squamous cell carcinoma").[61,62]

Clinically, AK typically present as superficial, keratotic, scaly, skin-colored, pink or white-yellow papules on sun-exposed skin (mostly in the head and neck area and on the dorsal hands). Multiple lesions are common. The diagnosis is typically made based on clinical examination. To rule out invasive growth (SCC), a punch biopsy should be performed in case of doubt (e.g. a painful lesion). An example is shown in Figure 3.

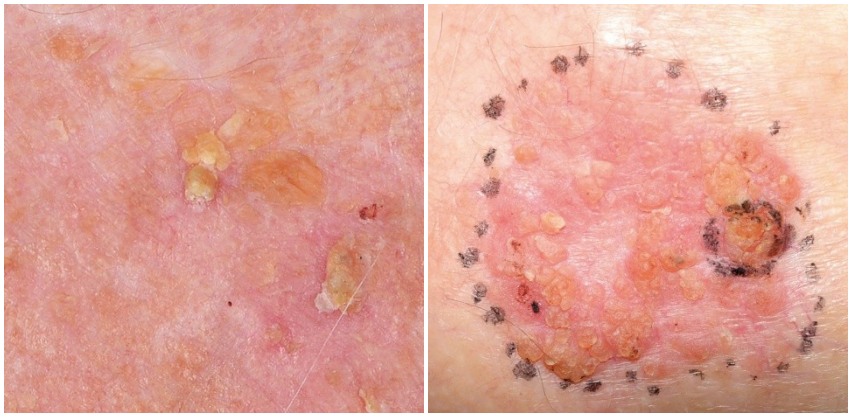
Although a relationship between AK and the development of SCC is generally accepted based on clinical, histopathological and genetic similarities, data regarding the exact progression rates are scarce. Most studies report a yearly progression rate per lesion of <1%. On the other hand, spontaneous regression of AK has also been reported (regression rates up to 63% of individual lesions). However, since multiple lesions (field cancerization) are often seen and it is not possible to predict which AK will transform into SCC, treatment is generally recommended.[61,62] Treatment options for AK include cryotherapy, photodynamic therapy, topical treatments (5-fluorouracil cream, imiquimod cream or ingenol mebutate gel), curettage, and laser therapy. Treatment choices are influenced by several factors, like the number of lesions, the body side distribution, and patient compliance.[61,62]

Bowen's disease (BD)

Incidence rates of BD are scarce and outdated (15-174 per 100 000 person-years; most studies >20 years old).[63] BD (or squamous cell carcinoma in situ) is histologically characterized by dysplasia throughout the entire (full-thickness) epidermis. Clinically, BD is

typically presenting as an hyperkeratotic, well-demarcated, erythematous papule or plaque (Figure 3), but several clinical variants are described (e.g. pigmented BD). In case of doubt a punch biopsy can confirm the diagnosis. Previous studies suggested a risk of progression from BD to SCC ranging from 3-5%. Treatment options include topical treatment with 5-fluorouracil cream, photodynamic therapy, local destructive therapies (e.g. cryotherapy or curettage with electrodesiccation), or surgical excision. In case none of these therapies are possible, radiotherapy may be an option.[63,64]

Figure 3 Examples of actinic keratosis (left) and Bowen's disease (right)



Cutaneous squamous cell carcinoma (SCC)

The incidence of SCC has been rising over the past decades and is also strongly related to increasing age.[41,43,45,47,48] In the Netherlands, age-standardized incidence rates increased from 22 up to 35 per 100 000 person-years in the period 1989-2008. As in BCC, this is probably an underestimation, mostly due to administrative reasons.[65]

SCC arises from keratinocytes in the epidermis and related appendages. Risk factors of SCC include: UVR-exposure (especially cumulative chronic sun exposure), chronic immunosuppression, increasing age, male sex, fair skin type (Fitzpatrick skin type I and II), previous skin cancer or precursor lesions, smoking, chronic inflammatory processes (e.g. lichen sclerosus), chronic wounds and burn scars, genetic predisposition (e.g. epidermolysis bullosa and oculo-cutaneous albinism), arsenic exposure, and previous PUVA or radiation therapy.[52,66,67] Some subtypes of human papillomavirus and Merkel cell polyomavirus are thought to contribute in the development of (a subset) of SCC as well, especially in chronic

immunosuppressed patients.[68] However, more research is needed to improve our understanding of a potential causative role.[68,69]

The clinical presentation of SCC usually consists of an indurated tumor with a keratinizing or crusted surface. Ulceration is common, especially in larger and/or less differentiated tumors. Examples are shown in Figure 4. SCC is growing faster and more aggressive as compared to BCC. Furthermore, SCC has a potential to metastasize, mostly to regional lymph nodes (±85%), although distant metastases are possible. Most studies report a 5-year metastatic risk ranging from 1-4% for low-risk SCC to a risk up to 10% in high-risk SCC, and even higher in specific subgroups of patients. Several factors are known to increase the risk for development of metastasis, of which the following are most commonly included in clinical practice guidelines: (1) SCC arising from the lip or ear, (2) SCC with a diameter ≥2 cm, (3) SCC with ≥ 4 mm depth growth, (4) undifferentiated or poorly differentiated tumors, (5) perineural or vasoinvasive tumor growth, (6) SCC in chronic immunosuppressed patients.[66,67,70,71]

Although clinically often suspected, a definite diagnosis is made by histopathological examination (after biopsy or excision), which includes the examination of the above-mentioned prognostic variables. To detect metastasis lymph node palpation should be performed, which is often complemented by ultrasound examination and ultrasound-guided aspiration (in case one or more suspicious lymph nodes are detected) in high-risk lesions.[66,67]

Figure 4 Examples of squamous cell carcinoma

In most cases SCC is treated by surgical excision, which allows histopathological control of the excision margins. Other treatment options which can be used in some cases are radiotherapy, cryosurgery or curettage with electrodesiccation.[66,67] As discussed in BCC, also in SCC and its precursor lesions adequate UVR-protection is considered an essential preventive measure.[66] More convincing evidence is available in favor of UVR-protection as preventive measurement in the development of SCC as compared to BCC and melanoma.[57] Follow-up examinations are usually scheduled for five years after a SCC, influenced by both patient and tumor characteristics (e.g. previous skin cancer, tumor stage, possibility to perform self-examination).

1.5.3 Cutaneous melanoma and precursors

The cutaneous melanoma is a malignant tumor arising from melanocytic cells in the skin. Although less frequent, melanoma can also arise from melanocytic cells in other organs (eye, meninges and various mucosae). In the further context of this thesis, extracutaneous melanoma are not included and only cutaneous melanoma are mentioned by the word melanoma. The most common precursor lesion of melanoma (melanoma in situ) is lentigo maligna, which is relatively common among older adults in chronically sun-exposed body sites.

Next to BCC and SCC, the incidence of melanoma is also increasing worldwide in Caucasians.[72,73] Multiple studies have shown the rise of incidence rates of melanoma is most pronounced among older adults.[73] Reported incidence rates range from <10 per 100 000 in some European populations to 50-60 per 100 000 in some Australian studies.[74] The most important exogenous risk factor for melanoma is UVR-exposure, especially sun burns. Other risk factors include: a total number of naevi >100, multiple (>5) atypical naevi, fair skin type, red or blond hair color, ephelides, blue eyes, large congenital naevi, actinically damaged skin, a history of NMSC, and genetic susceptibility (e.g. CDKN2A mutation).[52,72,74]

Four subtypes are used to classify melanoma: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma and acral lentiginous melanoma.[74] In older adults, the proportion of superficial spreading melanoma decreases and the proportion of the other forms seem to increase. Cutaneous melanoma in older adults are most commonly located in the head and neck region.[75] Melanoma have the potential to metastasize and cause death. Melanoma account for 90% of all deaths due to skin cancer and mortality rates related to melanoma are higher in older adults compared to younger populations, especially in males. Other prognostic factors of melanoma include: vertical tumor thickness (Breslow's depth; increasing thickness is related to a poorer prognosis), ulceration (related to poorer prognosis), the presence of dermal mitosis (related to poorer prognosis), level of invasion

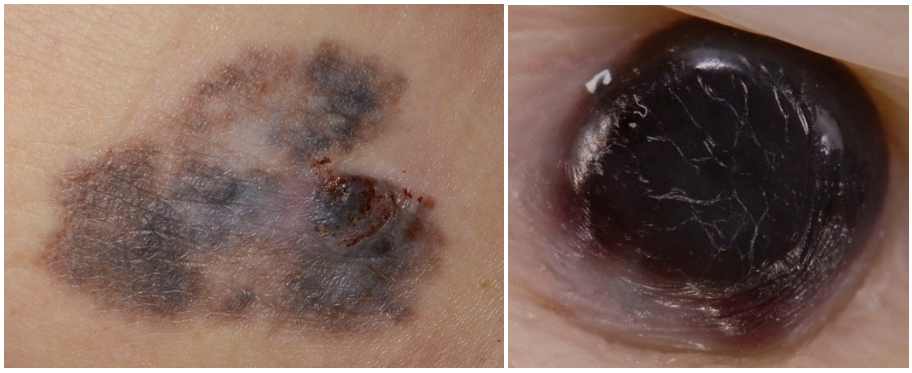
(Clark's level; increasing invasion is related to a poorer prognosis), and tumor location on the trunk or head and neck region (poorer prognosis compared to the limbs).[73,74] The poor prognosis of melanoma among older adults compared to younger patient groups is thought to be mainly caused by a late diagnosis and treatment. Examples of possible explanations for this delay are a lower awareness of skin cancer and the differences in subtype distribution among older adults.[73]

In case of a suspicion of a melanoma clinical examination is often complemented with dermoscopy. The ultimate diagnosis is made by histopathological examination after diagnostic excision. Excisional biopsy is preferred over incisional (punch) biopsy, due to the risk of sampling error and difficulties with establishing the Breslow's depth. Another hypothetical risk of incisional (punch) biopsy might be the induction of tumor spread, although evidence from current literature appears to be insufficient to support this statement.[74,76] The current guidelines recommend to use the staging system of the American Joint Committee on Cancer (AJCC) to classify melanoma.[72,77] After diagnostic excision, a sentinel-node biopsy is typically considered in melanoma stage IB or higher (melanoma with vertical tumor thickness >1 mm or ≤1 mm with ulceration and/or the presence of dermal mitosis). A sentinel-node biopsy includes histopathological examination of the first regional draining lymph node(s). This procedure mainly provides prognostic information, since the impact on prognosis is currently still controversial and a main topic of discussion in current literature.[72,74,78] Further staging in metastatic melanoma is usually performed, but seems out of the scope of this section.

Next, treatment consists of a therapeutical re-excision. An excision margin is chosen based on the Breslow's depth: 1 cm margin in tumors with a Breslow's depth <2 mm, 2 cm margin in tumors with a Breslow's depth ≥2 mm. Melanoma in situ is generally treated with an excision margin of 5 mm. Radiotherapy might be considered in inoperable cutaneous melanoma. In case of metastatic melanoma surgical excision (including lymph nodes dissection), radiotherapy and/or systemic therapy is usually performed.[72,74]

As discussed in BCC and SCC (including precursor lesions), also in melanoma adequate UVR-protection is considered an essential preventive measure.[74] Furthermore, patients are usually instructed how to perform self-examinations of the skin. Follow-up examinations are scheduled based on tumor stage and other patient characteristics like the ability to perform a self-examination and the presence of risk factors related to the development of subsequent skin tumors.

Figure 5 Examples of melanoma (left: superficial spreading melanoma, right: nodular melanoma)



1.5.4 Skin cancer care in frail older adults

Skin cancer care in frail older adults can be challenging in daily practice. Several patient- and tumor characteristics should be taken in consideration, including factors like prognostic tumor characteristics, a limited life expectancy, comorbidities, the impact on quality of life, and the treatment burden for a patient.

On the one hand, as described before, some highly prevalent skin cancer types (especially the low-risk NMSC) are slowly growing, rarely metastasize, and could stay asymptomatic for months. While on the other hand, the risk for local tissue destruction and related morbidity leading to a worse quality of life and even death in some cases, should not be underestimated. Furthermore, treatment in an early phase may be easily performed and result in a low patient burden, while the opposite may be increasingly seen with a longer delay. Balancing management decisions and the risk for under- and overtreatment is therefore essential, but not always easily performed.

1.6 Organisation of general long-term care in frail older adults in the Netherlands

Most older adults in the Netherlands live within their own houses (community-dwelling). Based on the extent and complexity of the care needed, an older adult may move to a permanent healthcare facility, which could be stratified into residential homes ("old people's homes") and nursing homes.[79] The number of residential homes in the Netherlands has decreased over the past couple of years, since governmental policy stimulates older adults

to keep living in their own homes longer.[80] Community-dwelling older adults and older adults living in residential homes are usually in need of some assistance in their activities of daily living and may be supported with basic (home) nursing, domestic and social services, an alarm service and provision of meals. These older adults usually receive primary medical healthcare by a general practitioner.[79,80]

Older adults living in nursing homes are in a need of more extensive and complex healthcare. Nursing home inhabitants usually are more frail and dependent compared to inhabitants of residential homes, and typically need help with most of their activities of daily living. In nursing homes primary medical healthcare is provided by an elderly care physician (previously called "nursing home physician" (NHP)), usually complemented by a multidisciplinary team of health-care professionals (e.g. physiotherapists, dietitians, and psychologists).[79,80]

1.7 Organisation of dermatologic care in the Netherlands

In the Netherlands dermatologic care is organized in three layers of care: primary, secondary, and tertiary medical care.

1.7.1 Primary dermatologic care

The first layer of dermatologic care (primary medical care) is provided by primary care physicians. Primary care physicians include general practitioners and elderly care physicians, depending on the living situation of an older adult, as discussed before. These primary care physicians are often referred to as "gatekeepers" of medical specialist care (secondary and tertiary care), since patients need a referral from a primary care physician before they can visit a dermatologist.[80] Skin diseases account for a significant part (12.7%) of the conditions seen by Dutch general practitioners.[81]

1.7.2 Secondary and tertiary dermatologic care

In general, the second and third layer of dermatologic care (secondary and tertiary care) are provided by dermatologists working within general hospitals (or private practices) and university hospitals, respectively.[80] University hospitals combine the provision of healthcare services with research and education. Although these hospitals do provide general dermatologic care, their main function is to provide top clinical and multidisciplinary dermatologic care services and expertise. This last resort function for referrals from dermatologists in general hospitals typically qualifies them as tertiary institutions.[82]

1.7.3 "Anderhalvelijnszorg"

During the last couple of years more and more attention has been paid to a new initiative called "anderhalvelijnszorg". In the context of dermatologic care, this concept may imply a dermatologist providing healthcare in a primary care practice. Such provision of secondary care in a primary care setting is assumed to be less expensive and a qualitatively equivalent method of healthcare provision compared to secondary (hospital-based) dermatologic care in some cases.

1.7.4 Teledermatology

Teledermatology is a form of e-health, in which a dermatologist is digitally consulted by another healthcare provider. This form of consultation mostly encompasses the use of a standardized questionnaire combined with photographs of a skin disorder, which are send through a secured internet connection. This type of teledermatology is often designated as "store-and-forward" (S&F) teledermatology. In the Netherlands, teledermatology has been increasingly used since the late nineties, especially by general practitioners.[83] Multiple studies showed that teledermatology is a highly efficient, cost-effective and easy-to-use consultation method.[84]

Moreover, previous research showed the use of S&F-teledermatology could prevent up to 68% of the referrals from general practitioners to dermatologists, which might result in a cost reduction of 18%.[85] Most studies indicated that the diagnostic accuracy and users satisfaction of S&F-teledermatology was acceptable in general, although face-to-face consultation was shown to have a superior accuracy. This accuracy may be limited by several aspects, including the type of skin condition. Several important logistical, legal and financial framework conditions are important to effectuate optimal implementation of teledermatological consultation. Potential (dis)advantages of S&F-teledermatology are summarized in Table 4.[83,84]

In addition, another form of teledermatology is real-time teledermatology (by video connection). This type of teledermatology includes live interaction between the users by means of a secured internet video connection. Real-time teledermatology may be able to overcome some of the limitations of S&F-teledermatology. For example, this type of teledermatology might improve diagnostic accuracy due to possibility to observe a skin lesion from different angles. Furthermore, it might be easier to obtain more information regarding the skin disease or patient's context with real-time teledermatology, since it is possible to ask additional questions and non-verbal communication can be observed. A potential logistical limitation of real-time teledermatology is that all users have to be available on the moment of consultation.[83]

Table 4 Potential (dis)advantages of store-and-forward teledermatology, modified from Lubeek et al.[83]

Potential advantages	
Accessibility	improvement of access to dermatologic care, which might be especially valuable in patients with physical and/or cognitive impairments limiting the possibility to visit a hospital
Efficiency	increased efficiency of dermatologic care, for instance because adequate treatment may be started earlier
Prevention of unnecessary referrals	prevention of unnecessary referrals to a dermatology outpatient clinic
Cost reduction	by minimizing diagnostic and treatment delay and the prevention of unnecessary referrals, total healthcare costs may be reduced
Education	providing an educational value, by facilitating the exchange of knowledge and experiences between users
Patient satisfaction	a comparable patient satisfaction was demonstrated in teledermatology compared to dermatology outpatient clinic visits
Potential disadvantages	
Diagnostic accuracy	a lower diagnostic accuracy, especially in case of a solitary (pigmented) lesion
Financial investment	e.g. purchase of the needed soft- and hardware, including a photocamera
Time investment	the time needed to prepare arrangements, to learn how to use teledermatology, and to learn how to make sufficient photographs
Dependency	the internet connection and soft- and hardware has to work properly
Limited information regarding the skin condition	the lack of live face-to-face interaction limits the possibility to obtain additional information regarding the skin condition, for instance by asking additional questions, by palpation of a skin lesion or by observing non-verbal communication
Limited information regarding the context of a patient	limits the possibility to "look beyond" the skin problem and gain information regarding the clinical and psychosocial context of a patient (e.g. general prognosis, comorbidities, cognitive impairment), needed to optimize a patient-specific management approach in some situations

1.8 Thesis aims and outline

Skin diseases are prevalent among older adults and healthcare providers are expected to be increasingly confronted with skin diseases in this population in the future, since the world population is aging rapidly. Skin diseases may have a significant impact on health-related quality of life. Little is known about the current need for, provision of, and quality of dermatologic care in the frailest older adult population (nursing home patients). One of the most common skin conditions dermatologists (and other healthcare providers) are confronted with in older adults is skin cancer and precursor lesions. Healthcare providers are regularly confronted with management dilemma's in this patient population in daily practice.

The aims of this thesis are:
I. To study the current need for, provision of, and quality of general dermatologic care among nursing home patients (Part A of this thesis)
II. To study current skin cancer care among older adults and to provide guidance in medical-decision making in skin cancer among older adults (Part B of this thesis)

Taking the above-mentioned aims into account, the following research questions were addressed (corresponding parts and chapters given between parentheses):

I. Dermatologic care in institutionalized older adults (Part A)

(1) What is the current need for and provision of dermatologic nursing home care according to nursing home physicians in the Netherlands? (**Chapter 2**)

(2) What is the current role of Dutch dermatologists in dermatologic care provision in nursing homes? (**Chapter 3**)

(3) What are the reasons and barriers for dermatologist consultations in nursing homes? (**Chapter 3**)

(4) How could we improve dermatologic care for nursing home patients? (**Chapters 2 and 4**)

II. Skin cancer care in frail older adults (Part B)

(1) What is the current and potential future role of nursing home physicians in the diagnosis and treatment of (pre)malignant skin lesions among nursing home patients? (**Chapter 5**)

(2) What is the influence of high age and comorbidities in medical decision making and guideline-adherence by dermatologists in older adults in daily clinical practice? (**Chapter 6**)

(3) What is currently known about the epidemiology and clinicopathological features of BCC in the oldest-old to guide healthcare providers and policy makers? (**Chapter 7**)

(4) Which items are considered important in medical decision making in frail older adults with NMSC and should be integrated in NMSC clinical practice guidelines? (**Chapter 8**)

(5) What is the extent of integration of these items in current NMSC clinical practice guidelines worldwide? (**Chapter 8**)

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PART A

Dermatologic care in institutionalized older adults

2

Current dermatologic care in Dutch nursing homes and possible improvements: a nationwide survey

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Abstract

Objectives

To assess the need for and provision of dermatologic care among Dutch nursing home patients and to obtain recommendations for improvement.

Design

Cross-sectional nationwide survey.

Setting

All 173 nursing home organizations in the Netherlands.

Participants

Physicians working in nursing homes.

Measurements

Web-based questionnaire concerning the burden of skin diseases in nursing home patients, diagnostic procedures and therapy, collaboration with dermatologists, physicians' level of education, and suggestions for improvement.

Results

A total of 126 (72.8%) nursing home organizations, with 1133 associated physicians participated in our study and received the questionnaire. A total of 347 physicians (30.6%) completed the questionnaire. Almost all respondents (99.4%) were recently confronted with skin diseases, mostly (pressure) ulcers, eczema, and fungal infections. Diagnostic and treatment options were limited due to a lack of availability and experience of the physicians. More live consultation of dermatologists was suggested as being important to improve dermatologic care. Other suggestions were better education, more usage of telemedicine applications, and better availability of diagnostic and/or treatment procedures like cryotherapy.

Conclusion

Physicians in nursing homes are frequently confronted with skin diseases. Several changes in organization of care and education are expected to improve dermatologic care in nursing home patients.

Introduction

With the rapidly aging of the world population, the number of older adults in need of long-term care is steadily increasing.[1-3] Although considerable differences between countries with regard to the organization of long-term care for older adults exist, all countries seem to share the primary goal to deliver the most appropriate care to this frail population.[4,5] In the Netherlands, older adults with multimorbidity and complex health problems generally live in nursing homes. Specially trained elderly care physicians (officially recognized as a medical discipline within the Netherlands since 1990) provide the medical care in these nursing homes.[6,7]

Skin diseases form a major health problem among institutionalized older adults[8-10] and could have a significant impact on quality of life.[11-13] The most common skin problems in institutionalized older adults are xerosis and eczema, fungal infections, (pressure) ulcers, and both benign as malignant skin tumors.[10,14-17] In all of these diseases both intrinsic (i.e. physiological skin maturation, resulting in a decrease or alteration of several functions) as extrinsic aging of the skin (e.g. photo-aging) often play an important role.[10] Furthermore, common geriatric problems including incontinence and an impaired mobility could be important etiologic factors in skin diseases among institutionalized older adults.[10,18,19]

Despite of the prevalence and the impact on quality of life, little is known about the need for and provision of dermatologic care in institutionalized older adults. The aim of this study was to assess the need for and provision of dermatologic care according to physicians in nursing homes. Furthermore, recommendations for improvement were obtained.

Methods

Questionnaire design

A 49-item web-based questionnaire was developed and pretested in several multidisciplinary brainstorming sessions attended by multiple elderly care physicians and dermatologists (n=24).

The main sections in the final questionnaire contained questions about the need for and provision of dermatologic care among nursing home patients, diagnostic procedures and therapy, collaboration between primary and secondary care providers, level of medical education, and suggestions for improvement. The diagnostic section included

dermatoscopy and punch biopsy as frequently used diagnostic procedures in dermatologic diseases. Because other frequently used diagnostics (i.e. laboratory tests and cultures) are widely available, these were not included in the questionnaire. The question types mostly used were 5-point Likert scales and multiple choice questions (examples are shown in Figure 1).

Figure 1 Examples of questions used in the questionnaire

How often were you confronted with a skin condition in your patients during the last three months?

- ☐ Never
- ☐ 1-3 times
- ☐ 4-6 times
- ☐ 7-9 times
- ☐ 10 times or more

Did you ever attend continuing medical education on a dermatology-related subject?

- ☐ Yes
- ☐ No

Study population and questionnaire administration

Data were collected between October 2013 and April 2014. All nursing home organizations within the Netherlands (n=173) were approached by telephone to give information about our study. When interested, the link to the web-based questionnaire was sent to a contact person (mainly a medical director), who further distributed the questionnaire to all physicians working in the organization. At least 2 attempts were made to contact an organization. All physicians working in nursing homes who were willing to participate were included (i.e. elderly care physicians, elderly care residents, and junior doctors). Approximately 4 weeks later a reminder was sent.

Statistical analyses

For numerical data, we calculated means and standard deviations (SD). Categorical data were expressed as numbers and percentages. We tested for selection bias due to non-response, comparing the age and gender of the respondents with the target population. Reference data about the target population were available only for elderly care physicians and elderly care residents because of limited availability of national registries.[20] In subgroup

analyses, we stratified the respondents based on years of experience (<10 years or ≥10 years). To examine the statistical significance of differences in responses, we used two-sample t-tests for numerical variables and χ^2 or Fisher's exact tests for categorical variables. Differences were considered to be statistically significant when P was less than 0.05. We used a complete case approach for analyses. Data analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 20.0 (IBM Corporation, Armonk, New York, United States).

Results

A total of 173 nursing home organizations were contacted, of which 126 (72.8%) were interested in participating. A total of 1133 physicians received the link to the web-based questionnaire, of which 362 (32.0%) completed the questionnaire. After exclusion of 15 non-physician respondents, 347 questionnaires (30.6%) were eligible for inclusion. Age and gender of the respondents showed no statistically significant differences compared with the target population, indicating representativeness regarding these characteristics (data not shown). Table 1 provides an overview of the respondent characteristics.

Need for and provision of dermatological care in nursing homes

Of the participants, 99.4% (n=345) were confronted with a dermatologic problem in 1 or more patients during the past 3 months, of which 62.5% (n=217) 10 times or more. Skin diseases most respondents were confronted with during the past 3 months were (pressure) ulcers (94.2%), eczema (88.2%), fungal infections (87.0%), pruritus sine materia (78.4%), bacterial infections (61.7%), and cutaneous (pre)malignancies (59.4%). A complete overview is shown in Figure 2.

Diagnostic procedures

Only few respondents had the possibility to perform dermatoscopic examination (6.1%) or punch biopsy (32.0%) within their organization. Furthermore, an even smaller number actually ever performed these diagnostic procedures and only a limited proportion of respondents had the possibility to ask a colleague to perform them. Subgroup analyses showed no significant differences based on years of experience. More detailed data are shown in Table 2. Finally, a considerable proportion of the responding physicians considered themselves completely incompetent to perform these diagnostic procedures (64.0% and 50.4%, respectively). A complete overview of the self-assessed competence is presented in Table 3.

Table 1 Responder characteristics of this cross-sectional nationwide survey among physicians in Dutch nursing homes to evaluate current dermatologic care (n=347)

Characteristics	Values
Age, mean (SD), y	43.9 (11.5)
Male gender, n (%)	105 (30.3)
Physician subgroup, n (%)	
Specialist	244 (70.3)
Resident	34 (9.8)
Junior doctor	59 (17.0)
Other	10 (2.9)
Experience in elderly care, mean (SD), y	11.8 (9.5)
Number of patients, mean (SD)	58.4 (25.8)

Abbreviations: SD, standard deviation; y, years.

Figure 2 Percentage of respondents confronted with different skin diseases in nursing home patients during the last 3 months

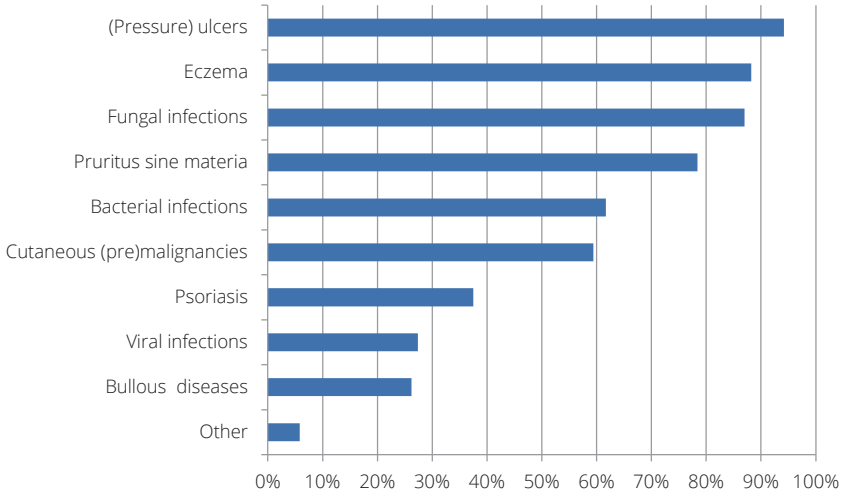


Table 2 Availability and performance of diagnostic procedures and treatment in skin diseases by physicians in Dutch nursing homes

	Available, %	Ever performed/prescribed, %			Possibility to ask colleague, %
		<10 YoE	*≥10 YoE*	*P-value*	
Diagnostics					
Dermatoscopy	6.1	4.5	3.7	0.697	9.8
Punch biopsy	32.0	14.4	16.4	0.607	33.1
Non-pharmacological treatments					
Incision	91.6	70.2	83.4	**0.004***	81.0
Excision	70.6	31.8	42.7	**0.04***	57.9
Curettage	40.6	18.0	20.5	0.559	32.6
Cryotherapy	38.3	23.2	27.3	0.390	38.3
Pharmacological treatments					
Topical:					
Antibacterials	NA	91.6	95.8	0.107	NA
Antifungals	NA	100.0	99.5	0.366	NA
Capsaicin	NA	18.1	36.3	**<0.001***	NA
Calcineurine inhibitors	NA	15.5	21.6	0.150	NA
Corticosteroids	NA	99.4	99.5	0.885	NA
Emollients	NA	96.8	95.8	0.633	NA
Fluorouracil	NA	38.4	65.6	**<0.001***	NA
Imiquimod	NA	12.3	16.3	0.287	NA
Vitamin D analogues	NA	40.0	45.3	0.326	NA
Systemic:					
Antibiotics	NA	94.2	98.9	**0.012***	NA
Antifungals	NA	65.2	84.2	**<0.001***	NA
Antiviral	NA	58.7	85.8	**<0.001***	NA
Prednisolone	NA	83.9	95.8	**<0.001***	NA

*Abbrevations: NA, not applicable; YoE, years of experience in elderly care. * p<0.05.*

Table 3 Self-assessed competence of physicians in Dutch nursing homes to perform several diagnostic and therapeutic procedures

	Level of competence, %				
Procedure	*Completely incompetent*	*Somewhat competent*	*Averagely competent*	*Above averagely competent*	*Completely competent*
Dermatoscopy	64.0	18.4	10.3	5.8	0.6
Punch biopsy	50.4	15.3	13.5	17.0	2.6
Incision	6.9	6.9	20.5	53.3	11.8
Excision	22.8	19.0	23.6	29.4	4.0
Curettage	46.4	17.3	16.4	14.7	3.7
Cryotherapy	25.4	15.9	20.5	30.5	6.9

Values may not add up due to rounding.

Non-pharmacological treatment

Non-pharmacological treatment options mostly available were incision (91.6%), excision (70.6%), curettage (40.6%), and cryotherapy (38.3%). Again, a smaller subset of respondents actually ever performed these treatment options themselves (76.1%, 37.2%, 18.7%, and 25.1%, respectively). Respondents with 10 years or more of experience were more likely to perform incision (59.5% vs. 40.5%, p=0.004) and excision (42.7% vs. 31.8%, p=0.04) than respondents with fewer than 10 years of experience.

A complete overview of data considering non-pharmacological treatment, including the possibility to ask a colleague and the self-assessed level of competence, is shown in Table 2 and 3, respectively.

Pharmacological treatment

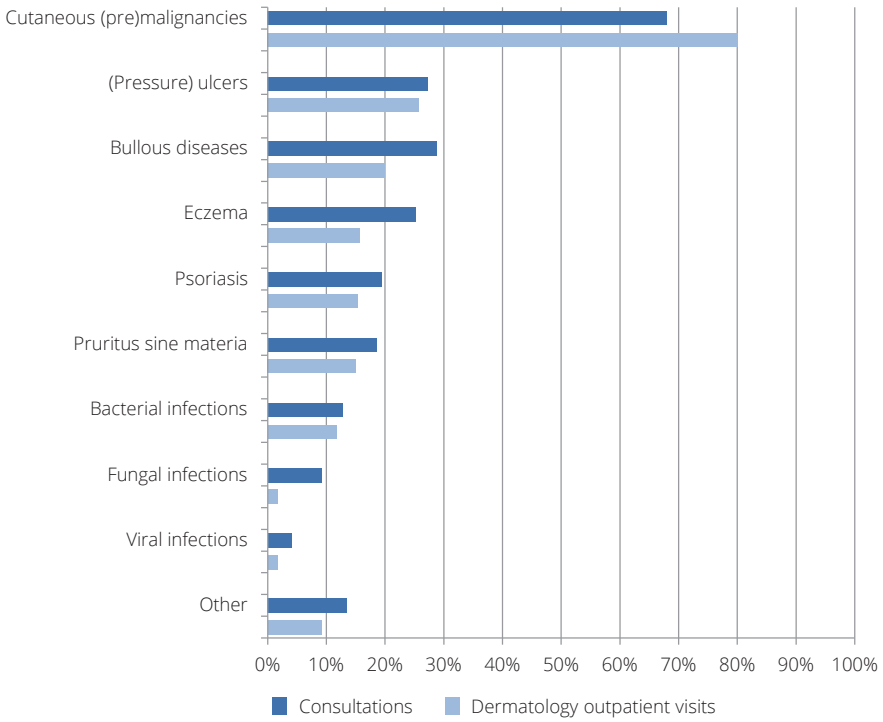
Topical treatments ever prescribed by the vast majority of respondents were corticosteroids (99.4%), antifungals (99.7%), emollients (96.3%), and antibacterials (93.9%). Subsequently, emollients, antifungals, and corticosteroids were also prescribed most frequently during the past 3 months (at least once a week by 85.3%, 72.0%, and 56.3% of the respondents, respectively). More experienced physicians were more likely to have ever prescribed capsaicin (36.3% vs. 18.1%, p<0.001) and 5-fluorouracil cream (65.6% vs. 38.4%, p<0.001) than physicians with fewer than 10 years of experience. Table 2 presents a complete overview of data, including systemic treatments.

Collaboration with dermatologists

Outpatient visits of nursing home patients

Most of the responding physicians (88.5%) indicated 1 or more of their patients visited a dermatology outpatient clinic during the past year. The most often reported reasons for these visits were cutaneous (pre)malignancies (80.1%), followed by (pressure) ulcers (25.7%), bullous diseases (19.9%), and eczema (15.6%). Figure 3 provides a complete overview of the reasons for dermatology outpatient clinic visits.

Figure 3 Percentage of respondents confronted with different skin diseases as a reason for dermatologist consultation and outpatient visits of nursing home patients during the past year



Several suggestions for improvements with respect to the outpatient clinic visits were made (n=117). Taking into account a patients general health status during medical decision-making more often was the most frequently made suggestion (33.3%), followed by more

communication between a dermatologist and the referring physician during the medical decision-making process (25.6%), better and/or more complete referral reply letters from dermatologists (23.9%) and to take into account the (logistical) limitations of a nursing home more often (4.3%).

Consultation of a dermatologist

More than three-quarters of the respondents (79.3%) consulted a dermatologist regarding 1 or more of their nursing home patients during the past year, of which 41.5% at least once every quarter of a year. The type of communication used by most of the respondents was a telephone conversation (76.4%), followed by telemedicine applications (31.6%), face-to-face consultation in a nursing home (31.3%), or e-mail (21.5%). The skin diseases most commonly named as a reason for these consultations are shown in Figure 3. More experienced physicians were more likely to have consulted a dermatologist during the past year compared with less experienced physicians (84.7% vs. 72.9%, p=0.007).

Management recommendations by dermatologists

The subsequent question focused on the amount of which several important patient-related factors (quality of life, multimorbidity, cognitive impairment, and (limited) life expectancy) are taken into account by dermatologists making medical management decisions in nursing home patients. Scores ranged from 1 to 5 (higher scores indicate taking the factor more into account). Data are shown in Figure 4. Quality of life received the highest score (mean (SD), 3.38 (1.07)), followed by multimorbidity (3.27 (1.00)), (limited) life expectancy (3.13 (1.07)), and cognitive impairment (2.97 (1.09)). All differences between the four patient-related factors were statistically significant with $p \leq 0.008$.

Dermatology (continuing medical) education

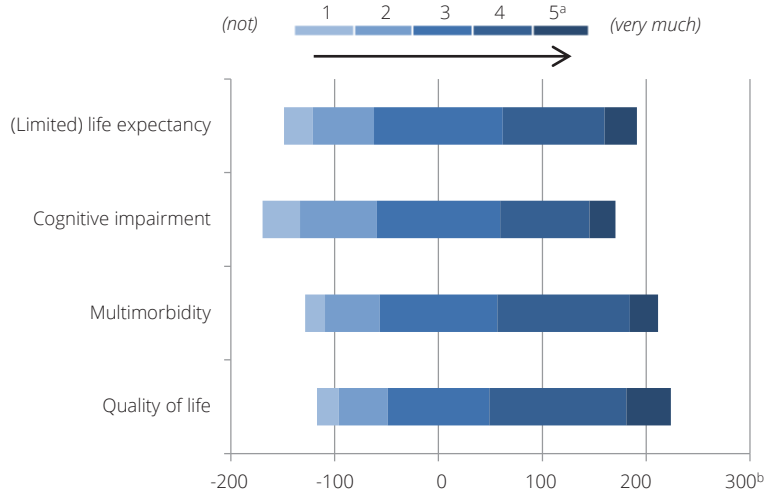
Basic training

Almost all respondents received basic training in dermatology during an undergraduate medical school course (95.7%) and/or clinical rotation (94.5%), irrespective of years of experience. Only a small minority received additional training during an elective dermatology course or clinical rotation (4.6% and 5.2%, respectively). Less experienced physicians were more likely to have attended an elective clinical rotation in dermatology compared to more experienced respondents (9.0% vs. 2.1%, p=0.004). The proportion of respondents who received an elective dermatology course during medical school was not influenced by years of experience.

Continuing medical education

Almost two-thirds of the participants (64.0%) had ever attended continuing medical education on a dermatology-related subject, of which (geriatric) dermatology in general was the most mentioned subject, followed by (pressure) ulcers (41.8%) and cutaneous (pre)malignancies (30.3%). More experienced physicians were more likely to have followed continuing medical education than less experienced physicians (85.8% vs. 37.4%, p<0.001).

Figure 4 The amount of which several patient-related factors are taken into account by dermatologists making medical management decisions in nursing home patients, according to physicians from Dutch nursing homes



[a] Scores ranged from 1 ("not") to 5 ("very much"), so higher scores indicated taking a factor more into account; [b] Number of physicians.

Demand for more education and suggested improvements of education

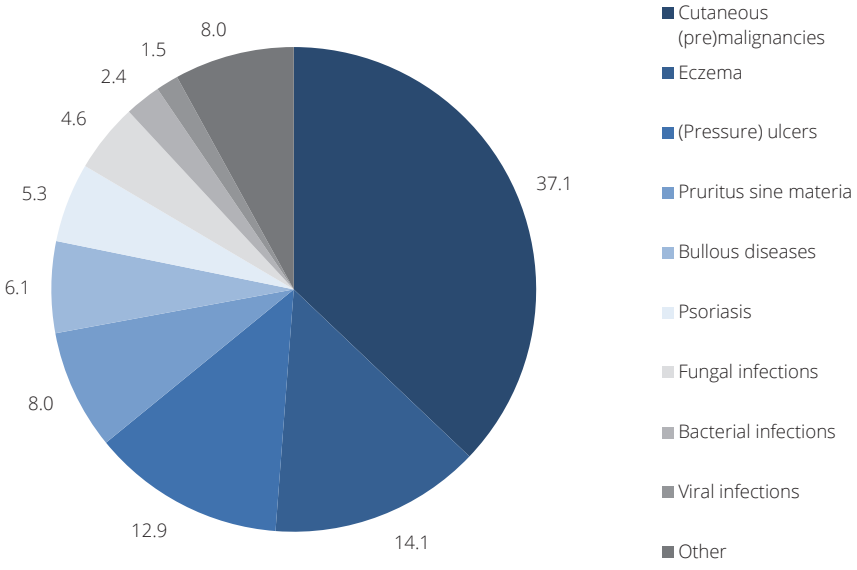
More continuing medical education was requested by 72.0% (n=250) of the responding physicians and 534 specific subjects were proposed. Suggested subjects could be divided in specific (groups of) dermatologic diseases (77.2%), (geriatric) dermatology in general (14.6%), and diagnostic/therapeutic skills (8.2%). Cutaneous (pre)malignancies were by far the most frequently (37.1%) mentioned subject among the specific (groups of) dermatologic diseases (Figure 5).

Next, the participants were asked in which way(s) education could be further improved. A total of 207 suggestions were made and the most common suggestion was more (specific) training focused on dermatology in older adults (42.5%), followed by more educational outreach visits (i.e. bed-side teaching) (23.7%), more online modules / e-learning (9.2%), the possibility to accompany a dermatologist in daily practice at an outpatient clinic (7.7%), more attention to dermatologic diseases in elderly care residency programs (4.9%) and subspecialty training of elderly care physicians with special interest in dermatology (2.4%).

Suggestions for general improvement of dermatologic care among nursing home patients

Most respondents (79.5%) reported suggestions to improve dermatologic care among nursing home patients in general. Of all suggestions (n=505), making more and better use of telemedicine applications (21.6%) and more consultation of dermatologists or dermatology nurses in nursing homes (21.4%) were most frequently suggested. Other suggestions were better availability of diagnostic and/or treatment procedures in nursing homes (15.8%), better clinical skills training (15.0%) and more knowledge about skin diseases in older adults (11.5%).

Figure 5 Specific skin diseases requested as topics for continuing education, in %



Discussion

Skin diseases are common among institutionalized older adults and could have a significant impact on quality of life.[8-13] Our study is the first to examine the need for and provision of dermatologic care among institutionalized older adults from the perspective of physicians in nursing homes. Almost all respondents (99.4%) were confronted with skin diseases in their patients on a regular basis and have experience with the most common pharmacological treatment options. However, diagnostic procedures and non-pharmacological treatment options are less commonly applied. Possible explanations shown in the present study are a lack of training and a lack of availability.

In this study (pressure) ulcers, eczema, and fungal infections were the most common skin diseases responding physicians were confronted with in institutionalized older adults. Nevertheless, cutaneous (pre)malignancies were the most frequently recorded reason to consult a dermatologist. Although the incidence of skin cancer is rising worldwide,[21,22] previous studies have shown a relative low incidence of skin cancer compared to other skin diseases among institutionalized older adults.[14-17] However, these studies were mainly conducted in non-Caucasian populations and some might be outdated. Limitations in experience with skin cancer and the earlier mentioned limited availability of diagnostic and treatment options could be other explanations for this frequent dermatologist consultation in skin cancer. Future research is needed to study this in more detail.

More and better usage of telemedicine applications was the most frequently made suggestions to improve current dermatologic care among nursing home patients. Previous studies showed telemedicine could improve nursing home care, might replace outpatient clinic visits and is generally accepted by patients, families, and caregivers.[23-29] Interestingly, most respondents in the present study (76.4%) used a telephone to consult a dermatologist, while telemedicine applications were used by relatively few respondents (31.6%). A possible explanation for this discrepancy could be a limited availability of telemedicine applications or a limited familiarity with telemedicine applications.

Although most participants in our present study received basic dermatology training, more and better training was requested by most of the respondents, especially educational outreach visits. More nursing home visits by dermatologists could be an option to partially meet these requests. Furthermore, more and better education could possibly result in lowering the threshold for a physician to obtain more experience in daily clinical practice and to improve the necessary (logistical) conditions (like the purchase of certain medical equipment).

To take into account a patient's general health status during medical decision making seems to be a suggestion to improve care of particular interest for dermatologists. Next to the earlier mentioned effects, a better and more intense collaboration between physicians in nursing homes and dermatologists could probably improve this item as well. Moreover, enough information about the patient's general health status, (end-of-life) treatment limitations, and the logistical (im)possibilities in a referral letter or consultation request to the dermatologist from the physician in a nursing home seems to be essential to create the required awareness among dermatologists for this item.

Limitations

There are several limitations in the present study. Non-physicians were not included in our study, because our questionnaire mostly focused on physician-specific items like prescription patterns and medical education. However, we acknowledge the increasing role of nurse practitioners and physician assistants in daily (dermatologic) care in nursing homes. Moreover, despite of our multidisciplinary brainstorming sessions and pretesting of the questionnaire, possible misinterpretation of some questions and the self-assessing character of the questionnaire might have influenced the results.

Conclusion

In conclusion, physicians working in nursing homes are frequently confronted with skin diseases in their patients and consultation of a dermatologist is requested on a regular basis. Better diagnostic and treatment facilities in nursing homes, better education, more usage of telemedicine, and more nursing home visits by dermatologists were designated as most important suggestions to improve dermatologic care in nursing homes.

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Dermatologic care of institutionalized older patients: a survey among dermatologists in the Netherlands

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Abstract

Background

Dermatologists are expected to be increasingly confronted with institutionalized older adult patients, due to the rapidly aging world population.

Objectives

To determine the proportion of dermatologists visiting patients in nursing homes, together with the reasons for consultation, barriers to perform these visits and diagnostic and treatment patterns.

Materials and methods

A web-based questionnaire regarding dermatologic care in nursing home patients was developed by a multidisciplinary group of dermatologists, residents and elderly care physicians. A cover letter containing a link to the final questionnaire was sent by e-mail to all 661 dermatologists and dermatology residents in the Netherlands.

Results

A total of 130 eligible questionnaires were returned (19.7%). Most respondents (79.2%) ever had contact with an elderly care physician concerning a nursing home patient. However, only 30.0% of the respondents ever visited a patient within a nursing home. The most common reasons for nursing home visits were cutaneous (pre)malignancies (51.4%), eczema/dermatitis (25.7%) and (pressure) ulcers (8.6%). The most important barriers mentioned to perform nursing home visits were a lack of time and indistinct and/or inadequate financial compensation. Diagnostic and treatment patterns often differed from the outpatient clinic due to various patient-related and logistic factors.

Conclusion

Dermatologists are frequently confronted with nursing home patients but only a minority visits patients within nursing homes. Lack of time and/or financial compensation seem important barriers.

Introduction

People aged 80 years and older (oldest-old) is the fastest growing age group worldwide and it is expected this age group will increase approximately sevenfold in the period 2013-2100, to 830 million people in 2100.[1] A considerable number of oldest-old people are in need of a permanent healthcare institution and the future demand for these institutions is expected to increase.[2-5] Although long-term older adult care differs around the globe, the concept of institutionalization of older adults in need of the highest level of care appears to be universal.[3-6] Within the Netherlands permanent healthcare institutions are classified into residential homes and nursing homes, depending on the type and extent of (medical) care needed. Older adults in need of the most complex care often live within nursing homes, where medical care is mainly provided by specially trained elderly care physicians.[7]

Skin problems form a significant part of care needed within permanent healthcare institutions.[8-11] The older adult skin is vulnerable to many skin problems due to both intrinsic and extrinsic aging. Intrinsic skin aging is caused by a physiological maturation of the skin, resulting in a decrease and alteration of several functions like immunosenescence, epidermal barrier function, and wound healing. Extrinsic aging is caused by environmental factors, of which exposure to ultraviolet radiation (photo-aging) is the most important.[12,13] Furthermore, frailty – defined as an increased risk of poor health outcomes due to vulnerability caused by a cumulative decline in multiple physiologic systems – but also more specific factors like immobility, multimorbidity, and cognitive impairment could affect the optimal detection and care of skin problems, especially in institutionalized older adults.[14-17] The most prevalent skin diseases affecting institutionalized older adults are xerosis, fungal infections, (pressure) ulcers, dermatitis, and skin tumors (both benign and malignant).[17-20] Skin problems may have a significant effect on quality of life in (institutionalized) older adults.[21-23] Consequently, consultation of a dermatologist in this vulnerable group of patients often seems desirable in daily practice. However, attending a dermatology clinic may not be feasible due to the various frailty-related factors mentioned before. In this situation a dermatologist visiting an institutionalized patient could be a solution.

Dermatologic care in the Netherlands can be distinguished in both primary, secondary, and tertiary care. Primary dermatologic care is mainly delivered by general practitioners or the previously mentioned elderly care physicians in the case of a nursing home patient. In contrast, both secondary and tertiary dermatologic care are delivered by dermatologists, within a general hospital (or medical specialist clinic) and academic hospital, respectively. Secondary and tertiary care is only available for a patient after referral of a primary care physician, to prevent unnecessary usage of medical specialist care.[24] Within the current

healthcare regulations dermatologists may visit patients outside of a hospital or clinic (for instance within a nursing home), although these regulations lack further specifications for this type of care and no nationwide arrangements are currently made to cover all nursing homes within the Netherlanders. Therefore, in case attendance of a nursing home patient to a dermatology clinic is not feasible, patients are dependent on primary dermatologic care, which could only be supplemented by secondary or tertiary dermatologic care if arrangements are made with one or more local dermatologists. Data regarding these visits of dermatologists to patients outside a hospital or clinic is currently missing in the literature.

This study aimed to determine the current proportion of dermatologists visiting institutionalized patients in nursing homes in the Netherlands, including reasons for consultation and barriers to perform these visits. Furthermore, diagnostic and treatment patterns were studied.

Methods

Development and composition of the questionnaire

The present, exploratory, cross-sectional, nationwide survey was performed using an anonymous web-based questionnaire intended for all dermatologists and dermatology residents within the Netherlands. We developed a 49-item questionnaire containing sections concerning the main outcomes: respondent characteristics, dermatologist consultation in nursing homes, diagnosis and treatment of skin diseases in nursing home patients, implementation of dermatologic care, decision-making in geriatric dermatology, and level of medical training. The questionnaire contained multiple choice questions, 5-point Likert scale questions (ranging from never to always), and open-ended questions. Concerning decision-making in geriatric dermatology, respondents were asked to score the amount of attention paid to four different items (quality of life, multimorbidity, cognitive impairment, and limited life expectancy) by themselves and by dermatologists in general, which are related to medical decision-making in older adult patients (in all clinical settings). The initial draft was extensively discussed and pretested in several multidisciplinary brainstorming sessions with multiple dermatologists, dermatology residents, and elderly care physicians.

Study population and distribution of the questionnaire

In March 2014 all dermatologists and dermatology residents within the Netherlands were approached by e-mail by the Dutch Society of Dermatology and Venereology, which

contained a cover letter and a link to the web-based questionnaire. A reminder e-mail was sent six weeks later.

Statistics

Continuous data were expressed as mean and standard deviation (SD) and categorical data were expressed as number and percentage. The age, gender, and physician subgroup (dermatologist or dermatology resident) of the respondent population were compared to the target population to test for selection bias due to non-response. Subgroup analyses were performed to determine the influence of the main respondent characteristics (age: <40 or ≥40 years; physician subgroup; and years of experience: <10 or ≥10 years) and whether a respondent visited nursing homes (yes or no) on some of the main outcomes: (willingness to perform) nursing home visits and level of medical training. A paired two-sample T-test was used to compare general with self-assessment scores, while an independent two-sample T-test was used to compare other continuous data. Categorical data were compared using a Chi-squared test (or Fisher's exact test in case any of the cells had an expected count of less than 5). We used a complete case approach and a p-value of <0.05 was considered statistically significant. All analyses were conducted using Statistical Package for Social Sciences (SPSS) for Windows, version 20.0 (IBM Corporation, Armonk, New York, United States).

Results

Respondent profile

Of the 661 dermatologists and dermatology residents who were invited by e-mail, 131 (19.8%) returned the questionnaire. No duplicate questionnaires were received. One questionnaire was excluded from further analysis because all answers with exception of the respondent characteristics were missing, resulting in 130 (19.7%) eligible questionnaires.

A comparison of age, gender, and physician subgroup between the respondent population and the target population showed no significant differences (data not shown), indicating an appropriate representativeness regarding these characteristics. Table 1 provides an overview of the baseline characteristics for respondents, separately specified for dermatologists and dermatology residents. The questionnaire was completed by 95 dermatologists (73.1%) and 35 dermatology residents (26.9%). The mean age (SD) of the respondents was 43.7 (11.0) years and a minority of the respondents (42.3%) was male. Dermatology residents were younger (mean (SD), 31.9 (3.1) years vs. 47.9 (9.6) years, p<0.001) and less often male (17.1% vs. 51.6%, p<0.001) compared to dermatologists.

Table 1 Baseline characteristics for respondents in our nationwide survey on dermatologic care in nursing homes

Characteristics	*Total (n=130)*	*Dermatologists (n=95)*	*Dermatology residents (n=35)*
Age, mean (SD), y	43.7 (11.0)	47.9 (9.6)*	31.9 (3.1)*
Male gender, n (%)	55 (42.3)	49 (51.6)*	6 (17.1)*
YoE, mean (SD)	NA	14.8 (10.5)	NA
Year of training, n (%)	NA	NA	1: 4 (11.4)
			2: 7 (20.0)
			3: 7 (20.0)
			4: 7 (20.0)
			5: 10 (28.6)

*Abbreviations: NA, not applicable; SD, standard deviation; y, years; YoE, years of experience. * p<0.001.*

Consultation in nursing home patients

Long-distance consultation

The majority of the respondents (79.2%) indicated they had contact with an elderly care physician to discuss 1 or more patients at some point in the past (correspondence by letter excluded), also shown in Table 2. Dermatologists were more likely to be contacted by an elderly care physicians compared to residents (87.4% vs. 57.1% respectively, p<0.001). No statistically significant differences in age or years of experience were observed. Regarding the methods of communication, most of those surveyed reported a telephone conversation (89.3%). Dermatologists more often used teledermatology applications or e-mail compared to dermatology residents (data shown in Table 2). For more than half of the participants (55.3%) these contacts took place at least 4 times a year. Most of the respondents (88.3%) indicated that it is sometimes or often possible to provide proper advice without live examination, but 7.8% rarely or never does this (3.9% were missing). An overwhelming majority (92.2%) of respondents which were contacted by an elderly care physician in the past indicated there had been patients for whom they believed it would have been better when they were consulted earlier: 15.5% even reported this often happened.

Nursing home visits

A total of 39 respondents (30.0%) reported that they had visited 1 or more patient(s) in a nursing home at some point in the past. None of the dermatology residents visited a

nursing home patient before. Dermatologists who visit nursing homes were more likely to be older (89.7% ≥40 years old vs. 67.9% ≥40 years old, p=0.013) and more experienced (82.1% ≥10 years of experience vs. 59.2% ≥10 years of experience, p=0.021) than those who never visited a nursing home. Of the dermatologists who had visited 1 or more patients within a nursing home in the past year, over half (54.3%) did so at least 4 times a year. For an overview of all data regarding consultation and nursing home visits, shown in Table 2.

Over two thirds of the participants (68.5%) are willing to visit patients on location within a nursing home (for the first time or more often when already performed a visit in the past). Interestingly, respondents who are willing to perform (more) visits were more likely to be younger (81.8% vs. 58.1%, for respondents aged <40 years old vs. ≥40 years old, p=0.004), to have less years of experience (77.8% vs. 55.7%, for respondents with <10 years of experience vs. ≥10 years of experience, p=0.049) and to be a resident (88.6% vs. 61.1%, for dermatology residents versus dermatologists, p=0.003). There was no difference in willingness between respondents who visited nursing homes in the past and those who did not. Among the respondents not willing to perform nursing home visits, most mentioned a lack of time to perform visits (80.5%) and indistinct and/or inadequate financial compensation (34.1%) as reasons. Of the dermatologists who visited patients in a nursing home during the past year, 51.4% reported (suspected) cutaneous (pre)malignancies as the most common reason for consultation, followed by eczema/dermatitis (25.7%). Figure 1 provides a complete overview of these data.

Figure 1 An overview of skin diseases reported as most common reasons for nursing home visits by dermatologists, in %

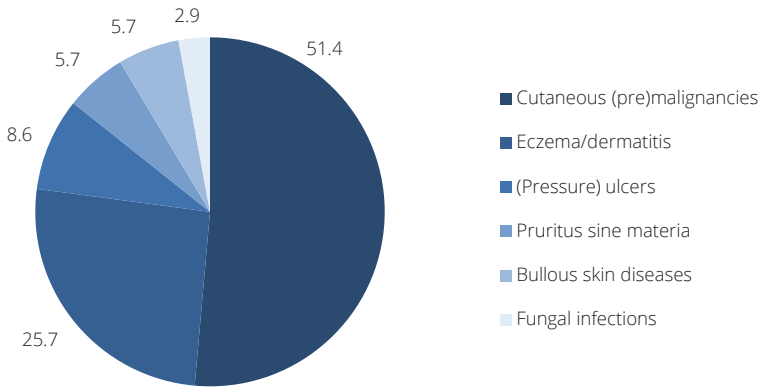

Table 2 Consultation and nursing home visits of dermatologists and dermatology residents

Total activities	*Total number of respondents (n=130)*	*Dermatologists (n=95)*	*Dermatology residents (n=35)*	*P-value*
Had contact with an elderly care physician, n (%)[a]	103 (79.2)	83 (87.4)	20 (57.1)	**<0.001***
Visited a patient in a nursing home, n (%)[a]	39 (30.0)	39 (41.1)	0 (0)	**<0.001***
Willing to visit nursing homes (more often), n (%)	89 (68.5)	58 (61.1)	31 (88.6)	**0.003***
Consultations	*Number of respondents (n=103)*	*Dermatologists (n=83)*	*Dermatology residents (n=20)*	*P-value*
Proportion of the respondents using different methods of communication, n (%)[b]:				
Telephone	92 (89.3)	72 (86.7)	20 (100)	0.085
Teledermatology applications	38 (36.9)	38 (45.8)	0 (0)	**<0.001***
E-mail	33 (32.0)	31 (37.3)	2 (10.0)	**0.019***
Other	9 (8.7)	9 (10.8)	0 (0)	0.123
Frequency of contact with elderly care physician in the last year, n (%):				
0 times	3 (2.9)	3 (3.6)	0 (0)	**<0.001***
1-3 times	43 (41.7)	25 (30.1)	18 (90.0)	
4-6 times	23 (22.3)	23 (27.7)	0 (0)	
7-9 times	11 (10.7)	9 (10.8)	2 (10.0)	
10 times or more	23 (22.3)	23 (27.7)	0 (0)	

Table 2 Consultation and nursing home visits of dermatologists and dermatology residents (continued)

Nursing home visits	*Number of respondents (n=39)*	*Dermatologists (n=39)*	*Dermatology residents (n=0)*	*P-value*
Frequency of nursing home visits in the last year, n (%):				
0 times	4 (10.3)	4 (10.3)	NA	NA
1-3 times	16 (41.0)	16 (41.0)		
4-6 times	8 (20.5)	8 (20.5)		
7-9 times	5 (12.8)	5 (12.8)		
10 times or more	6 (15.4)	6 (15.4)		
Number of nursing home locations visited in the last year, n (%):				
1	18 (51.4)	18 (51.4)	NA	NA
2	9 (25.7)	9 (25.7)		
3 or more	7 (20.0)	7 (20.0)		
Type of nursing home visits in the last year, n (%):				
Planned/standardized visits	18 (51.4)	18 (51.4)	NA	NA
Ad hoc visits	16 (45.7)	16 (45.7)		
Both	1 (2.9)	1 (2.9)		

Table 2 Consultation and nursing home visits of dermatologists and dermatology residents (continued)

Nursing home visits	*Number of respondents (n=39)*	*Dermatologists (n=39)*	*Dermatology residents (n=0)*	*P-value*
Present during nursing home visits in the last year, n (%):				
Elderly care physician	30 (85.7)	30 (85.7)	NA	NA
Nursing staff	32 (91.4)	32 (91.4)		
Dermatology nurse	5 (14.3)	5 (14.3)		

*NA, not applicable. Values may not add up due to missing values and rounding. [a] At some point in the past; [b] Contact by letter excluded; * p<0.05.*

Diagnosis and treatment within nursing homes

Diagnostic procedures

The majority of the dermatologists visiting nursing homes (82.9%) performed diagnostic procedures within a nursing home, of which punch biopsy (65.7%) and dermatoscopic assessment (62.9%) are the most common procedures used, followed by the collection of tissue samples to detect pathogenic micro-organisms (45.7%), and (ordering) blood tests (40.0%).

Among the respondents visiting nursing homes, 91.4% confirmed that there were differences between the diagnostic procedures performed within a nursing home compared to the outpatient clinic. More specifically, a less frequent usage of diagnostic procedures within nursing homes was most often mentioned (81.3%), followed by no performance of diagnostic procedures in nursing homes at all (12.5%). The remaining 6.2% reported to use other diagnostic procedures within nursing homes. The most common reasons for these diagnostic differences were: a limited life expectancy of the patient (68.8%), excessive burden for the patient (62.5%), unavailability of diagnostic procedures (53.1%), physical impairment of the patient (40.6%), requested by the patient or relatives (40.6%), cognitive impairment of the patient (34.4%), requested by the elderly care physician involved (28.1%), and a lack of supporting staff (21.9%).

Dermatological treatment

Non-pharmacological treatment in a nursing home was performed by 80.0% of the respondents visiting nursing homes, of which cryotherapy (68.6%) was most commonly applied, followed by shave excision or curettage (40.0%), surgical excision (22.9%), mechanical debridement (22.9%), UVB phototherapy (8.6%), and electrodesiccation (5.7%).

All dermatologists indicated their treatment decision sometimes differed within a nursing home compared to the outpatient clinic. Almost half of the participants reported to perform less treatment or no treatment at all (43.8%), followed by use of other treatment options (28.1%). The most common reasons for the treatment differences mentioned were: requested by the patient or relatives (65.7%), excessive burden for the patient (60.0%), a limited life expectancy of the patient (54.3%), physical impairment of the patient (51.4%), unavailability (40.0%), requested by the elderly care physician involved (37.1%), cognitive impairment of the patient (28.6%), a lack of supporting staff (22.9%), and an expected increased risk to develop complications (22.9%).

Implementation of dermatologic care

The recommendations given by the dermatologists visiting nursing homes were often (45.7%) or always (45.7%) properly followed according to most of the respondents, while one respondent (2.9%) indicated given recommendations were only sometimes properly followed and two respondents (5.7%) did not know. The reasons suggested for the incorrect implementation of recommendations by most respondents were non-compliance and/or misunderstanding of the nursing staff (70.6%), the elderly care physician (38.3%), or the patient (11.8%). Furthermore, 29.4% of the respondents indicated a delayed delivery or no delivery of medication as a reason.

Decision-making in geriatric dermatology

Regarding the items on decision-making in geriatric dermatology, almost all of the respondents (96.9%) gave themselves a high score (4 or 5 out of 5) on "taking quality of life into account", resulting in a mean score (SD) of 4.4 (0.6). All other items were scored significantly lower (3.7-4.0, p≤0.001). When dermatologists were scored in general, they received significantly lower scores on all items compared to the self-assessment (p≤0.001). The scores for dermatologists in general were significantly lower given by dermatology residents compared to dermatologists on "taking quality of life into account" (mean (SD), 3.47 (0.75) vs. 3.93 (0.76), p=0.003) and "taking comorbidities into account" (mean, (SD), 3.41 (0.74) vs. 3.71 (0.67), p=0.003). All of the items scored by the respondents are summarized in Table 3.

Table 3 Scoring of items taken into account by respondents during medical decision-making (5-point scale, higher scores suggest items are taken more into account)

Items	*Self-assessment scores*	*Scores for dermatologists in general*	*Difference (95% CI)*
Quality of life, mean (SD)	4.4 (0.6)	3.8 (0.8)	0.6 (0.50.7)*
Multimorbidity, mean (SD)	4.0 (0.7)	3.6 (0.7)	0.4 (0.3-0.5)*
Cognitive impairment, mean (SD)	3.7 (0.9)	3.5 (0.7)	0.2 (0.1-0.4)*
(Limited) life expectancy, mean (SD)	4.0 (0.9)	3.5 (0.8)	0.5 (0.4-0.6)*

*Abbreviations: 95% CI, 95% confidence interval; SD, standard deviation. * p≤0.001.*

Level of training

A minority of the participants received training in geriatrics during medical school (44.6%). Furthermore, 41.5% of the participants received training during the medical internship years and only 28.5% received training during continuing medical education activities. Nevertheless, the majority of the respondents (83.8%) considered themselves sufficiently trained to provide an adequate level of dermatologic care in nursing home patients. Dermatology residents were less likely to consider themselves sufficiently trained compared to dermatologists (65.7% vs. 90.5%, $p<0.001$), while no statistically significant influences of age and years of experience were observed. Furthermore, respondents who visited nursing homes in the past more often considered themselves sufficiently trained compared to those who did not (100% vs. 78.0%, $p=0.002$).

The main subjects of which a lack of training and/or knowledge was reported were geriatric medicine in general (22.6%), polypharmacy (22.6%), multimorbidity (19.4%), and skin cancer care in older adult patients (9.7%). Furthermore, half of the respondents (50.8%) would like to receive more training in geriatrics.

Discussion

To the best of our knowledge the present study is the first to examine the nationwide need for and provision of dermatologic care in institutionalized older adults. Our study shows a high demand for dermatological care among frail institutionalized older adults. In accordance with these present results, previous studies also showed a considerable demand for consultation within permanent healthcare institutions by different medical specialists. Furthermore, the availability of a consultant service by medical specialists could improve medical care in nursing homes.[25-26]

The most common skin diseases affecting institutionalized older adults generally correspond with the most common reasons for consultations in nursing homes by dermatologists found in our study. However, we found a strikingly high portion of cutaneous (pre)malignancies as a reason for consultation.[17-20] Possible explanations for this finding could be the ongoing rise of incidence of skin cancer worldwide,[27-28] a lack of knowledge and/or experience in diagnosing and treating cutaneous (pre)malignancies among elderly care physicians, and/or inadequate logistical possibilities for the latter. Considering the potential morbidity and mortality of cutaneous (pre)malignancies, timely diagnosis and treatment is considered important. Therefore, future research should focus more

extensively on skin cancer care in institutionalized older adults, including the role and training of elderly care physicians and/or specialized nurses.

Another important finding in our study was that the majority of dermatologists and dermatology residents is willing to visit institutionalized patients when indicated. However, at present only a minority actually performs visits to nursing homes. Lack of time and financial compensation were stated as major explanatory factors for this mismatch. Potential other factors which could possibly influence the mentioned willingness to visit institutionalized patients are a lack of an adequate infrastructure (both technically as personally) and a lack of a proper and uniform documentation system. More attention for these aspects by healthcare policymakers seems to be important in order to optimize care and meet the expected increase in frail older adults living in permanent healthcare institutions, in which an outpatient visit to a dermatology clinic often may not be feasible.

Finally, this study shows that several diagnostic and treatment procedures are less frequently used within nursing homes as compared to outpatient clinics. This can be explained by multiple factors, as indicated by the respondents in this study. First, patient-related factors, such as an excessive burden for the patient or a limited life expectancy of institutionalized older adults, could make a dermatologist less prone to perform (extensive) diagnostic or treatment procedures. In addition, several logistic factors, such as unavailability of procedures and a lack of supporting staff, are also mentioned as reasons for the less frequently usage of diagnostic and treatment procedures. The latter could be an important limitation to deliver the optimal dermatological care within this population.

In conclusion, this nationwide survey showed few dermatologists visit institutionalized patients within a nursing home when an outpatient appointment is not feasible, despite the frequent confrontation with this frail group of older adults and a considerable willingness to perform these visits. Several, mainly logistic factors were stated as limitations in dermatologic care.

Limitations

A limitation of this study is the relatively low response rate, resulting in possible selection bias. This could for instance have led to a potential overestimation of the proportion of dermatologists visiting nursing homes. Nevertheless, it is reassuring we found no significant differences in baseline characteristics between respondents and the target population. In addition, despite of our thorough multidisciplinary questionnaire development process, the partial self-assessing character of some questions and the possibility of misinterpretation could have influenced the results.

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4

Improving dermatological care for older adults living in permanent healthcare institutions: suggestions from Dutch dermatologists

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Introduction

Dermatologists are increasingly confronted with frail, institutionalized older adult patients, as the world population is aging rapidly and the demand for permanent healthcare institutions is growing.[1, 2] Skin problems are common among institutionalized older adults and can have a significant impact on quality of life.[3–6] Furthermore, dermatological care can be challenging and the possibility to visit an outpatient dermatology clinic may be limited within this population due to factors such as immobility, multimorbidity, and cognitive impairment. The aim of this study was to investigate possible ways to improve dermatological care in this vulnerable population.

Methods

In 2014, dermatologists and dermatology residents in the Netherlands were asked for suggestions to improve dermatological care in institutionalized older adults in a nationwide web-based survey of geriatric dermatology. Baseline characteristics and years of experience (or training in case of a resident) of respondents were included. Suggestions were categorized into several topics. Data analyses were performed using Statistical Package for Social Sciences (SPSS, version 20.0, IBM Corporation, Armonk, New York, United States).

Results

Respondent characteristics are shown in Table 1. In total, 83 (63.8%) dermatologists and dermatology residents suggested 149 possible ways to improve dermatological care among institutionalized older adults.

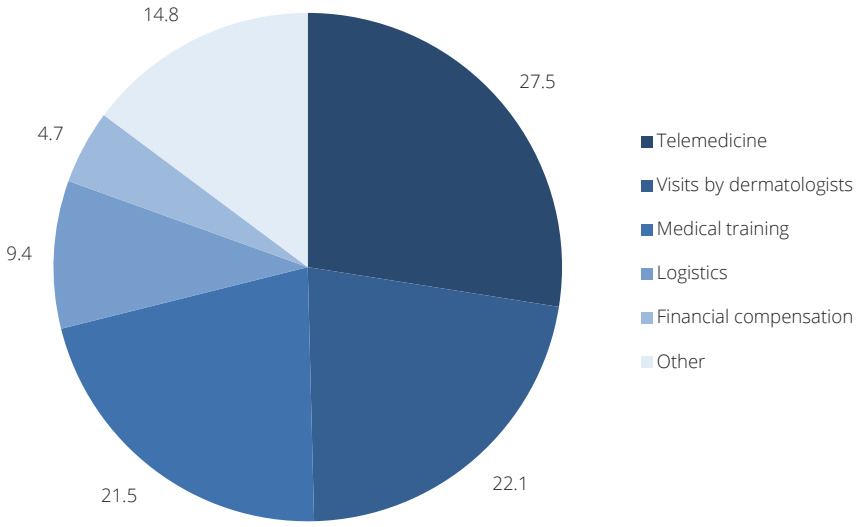
The most commonly made suggestions were: more and/or better utilization of telemedicine applications (27.5%), more visits to permanent healthcare institutions by dermatologists when indicated (22.1%), and more and/or better medical training of healthcare providers (21.5%). According to most respondents medical training should be targeted especially at elderly care physicians (78.1%), nursing staff (15.6%) and, to a lesser extent, dermatologists (6.3%). An overview of the suggested items is shown in Figure 1.

Table 1 Baseline characteristics for respondents to a web-based survey considering geriatric dermatology

Characteristics	*Total (n=83)*	*Dermatologists (n=59)*	*Dermatology residents (n=24)*
Age, mean (SD), y	42.9 (10.6)	47.1 (9.3)	32.0 (3.4)
Male gender, n (%)	33 (39.8)	30 (50.8)	3 (12.5)
YoE, mean (SD)	NA	13.8 (8.7)	NA
Year of training, n (%)	NA	NA	1: 3 (12.5)
			2: 4 (16.7)
			3: 4 (16.7)
			4: 5 (20.8)
			5: 8 (33.3)

Abbreviations: NA, not applicable; SD, standard deviation; y, years; YoE, years of experience.

Figure 1 Suggestions (n=149) for improvement of dermatologic care in permanent healthcare institutions, arranged by topic, in %



Discussion

This study provides some important suggestions to improve dermatological care in the institutionalized older adult population. This is essential due to the growing population of older adults who depend on institutionalized healthcare worldwide, and the high prevalence of skin problems within this vulnerable population.

More and/or better utilization of telemedicine was the most common suggestion made. Several studies have shown that telemedicine applications could be of great value in improving medical care in institutionalized older adults and have a positive effect on healthcare efficacy, quality of life, and a reduction in healthcare costs. The acceptance and feasibility of telemedicine applications were observed to be excellent among patients and caregivers.[7–10] Furthermore, both Zelickson & Homan[7] and Binder et al.[8] showed that teledermatology consultations were able to replace some outpatient clinic visits.

Secondly, more visits to permanent healthcare institutions by dermatologists was another commonly made suggestion, which seems to be in concordance with previous studies showing considerable demands for consultation by different medical specialists and that availability of a consultant service by specialists could improve medical care for institutionalized older adults.[11,12]

The final commonly made suggestion was more and better training of healthcare providers, especially elderly care physicians. This is despite the fact that basic dermatological training is currently included in most specialist training programmes for elderly care physicians across the Netherlands. A previous study showed a considerable demand for more and better continuing medical education among nursing home physicians, which emphasizes the importance of further development of educational programmes in the future.[13] Finally, the Dutch Order of Medical Specialists is currently focussing more attention on older adult care in medical specialty training, including dermatology.[14]

In conclusion, more (telemedicine) consultations and better medical training of healthcare providers seem important ways to improve dermatological care in permanent healthcare institutions. Researchers, health policymakers, and physicians should focus their future directions on these aspects.

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PART B

Skin cancer care in frail older adults

5

Skin cancer care in institutionalized older adults in the Netherlands: a nationwide study on the role of nursing home physicians

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Abstract

Background

The role of nursing home physicians in skin cancer care in institutionalized older adults is expected to increase in the future.

Objectives

To study the current role of nursing home physicians in skin cancer care among nursing homes in the Netherlands and to identify recommendations for improvement.

Methods

We conducted a cross-sectional nationwide study among nursing home physicians in the Netherlands using an anonymous self-administered online questionnaire.

Results

The knowledge and experience of nursing home physicians in diagnosing skin cancer appeared to be limited and dermatologists are frequently consulted. Some respondents have treated a (pre)malignant skin lesion themselves in the past on their own initiative (37.8%) or after consultation of a dermatologist (57.6%). Most of the nursing home physicians (94.5%) were willing to perform more treatment in one or more subtypes of (pre)malignant skin lesions after more education. More visits of dermatologists to nursing homes and more usage of telemedicine applications were other frequently suggested improvements.

Conclusion

The current limited role of nursing home physicians in skin cancer care in institutionalized older adults could be extended by more education. The role of the dermatologist remains essential and more possibilities for (live) consultation of dermatologists is expected to improve current care.

Introduction

Skin cancer is common within the oldest-old (people aged 80 years and older) and the incidence is still rising.[1-6] Although mostly nonlethal, the mortality rates of both melanoma[1,2] as nonmelanoma skin cancer are higher in de oldest-old compared to the overall population.[7,8] Furthermore skin cancer may cause substantial morbidity, due to infiltration and destruction of adjacent tissues and/or metastasis.[9-11]

Considering that the oldest-old form the fastest growing age group worldwide and that a significant part of this vulnerable group is in need of permanent institution-based healthcare,[12-16] the role of physicians working in these institutions in managing skin cancer is expected to increase as well.

There are several differences between nations regarding the organization of permanent healthcare facilities.[14,17] Residential homes and nursing homes are the two main types of permanent healthcare institutions in the Netherlands, discriminated by the type and extent of care needed. Older adults living within nursing homes are generally in need of the most complex care, which is supplied and coordinated by nursing home physicians (NHPs).[18]

Previous studies of our group showed that (pre)malignant skin lesions are one of the most common skin diseases NHPs are confronted with in nursing home patients (59.4% during the last three months).[19] Subsequently, (pre)malignant skin lesions were the main reason for dermatologist consultation, referral to an outpatient dermatology clinic or a nursing home visitation by a dermatologist.[20] Skin cancer care in institutionalized older adults could be complicated and limited by several factors such as multimorbidity, cognitive impairment, a limited life expectancy, and logistic factors (for instance a diminished ability to visit a hospital due to physical impairment). Furthermore, the level of knowledge and skills of caregivers seems to be another factor of great influence on medical care.[19]

Primary objective of this study was to assess the current role of NHPs in the diagnosis and treatment of different (pre)malignant skin lesions among institutionalized older adults living in nursing homes across the Netherlands. Secondary objectives were to assess the collaboration with dermatologists, the potential influence of education, and to collect recommendations for improvement of skin cancer care among institutionalized older adults.

Methods

Questionnaire development and study population

Data were obtained from a nationwide cross-sectional study among NHPs in the Netherlands. We used an anonymous self-administered web-based questionnaire with a dedicated section on skin cancer care, which was analyzed in this study.

Subtypes of (pre)malignant skin lesions included were: actinic keratosis (AK), Bowen's disease (BD), basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma. Treatment options included were: cryotherapy, surgery (including curettage/shave and/or electrodessication), radiotherapy, topical 5-fluorouracil, topical imiquimod, and photodynamic therapy. Methods were more extensively described in our previous study.[19]

Statistical analysis

Continuous data were expressed as mean and standard deviation. Categorical data were expressed as number and percentage. Representativeness of the respondents compared to the target population was tested by comparing age and gender. Subgroup analyses were performed to determine the influence of years of experience (<10 years or ≥ 10 years) and continuing medical education (CME) concerning (pre)malignant skin lesions in de past (yes or no) on the main outcome measures. Continuous and categorical variables were compared using an unpaired two-sample T-test and a Chi-squared test respectively. A difference was considered to be statistically significant when $p<0.05$. A complete case approach was used. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS®) for Windows, version 20.0 (IBM Corporation, Armonk, NY).

Results

Questionnaire distribution and response

A total of 126 out of 173 nursing home organizations approached consented to participate (72.8%). An e-mail invitation with a link to the online questionnaire was spread among the 1133 associated NHPs, of which 347 (30.6%) completed the questionnaire. A comparison of age and gender between the responding NHPs and the target population showed no significant differences, indicating an appropriate representativeness regarding these factors. The demographics and baseline characteristics of the respondents are shown in Table 1.

Table 1 Responder characteristics in this nationwide, cross-sectional study among nursing home physicians (NHPs) in the Netherlands (n=347)

Characteristics	Values
Age, mean (SD), y	43.9 (11.5)
Male gender, n (%)	105 (30.3)
Physician subgroup, n (%)	
Specialist	244 (70.3)
Resident	34 (9.8)
Junior doctor	59 (17.0)
Other	10 (2.9)
Experience in elderly care, mean (SD), y	11.8 (9.5)

Abbreviations: NHPs, nursing home physicians; SD, standard deviation; y, years.
Values may not add up due to missing values and rounding.

Diagnosis

The vast majority of the NHPs considered their knowledge to be sufficient to recognize AK (81.8%) and BCC (78.1%). A small majority considered their knowledge to be sufficient to recognize SCC (53.3%) and melanoma (54.5%), whereas a minority of the respondents considered their current level of knowledge to be sufficient to recognize BD (18.2%). Data are also shown in Table 2. Years of experience did not have a statistically significant influence on these results. Respondents who followed CME concerning (pre)malignant skin lesions considered their knowledge more often sufficient to recognize all subtypes with the exception of AK compared to their colleagues who didn't follow CME concerning this subject (all $p<0.05$). A complete overview of data is given in Supplemental Table S1.

Treatment

A minority of the responding NHPs considered their knowledge sufficient to perform treatment in the different subtypes, shown in Table 2. We did not observe differences in knowledge considering treatment between the NHPs with <10 years experiences and those with ≥10 years experience. NHPs who followed CME concerning (pre)malignant skin lesions considered their knowledge more often sufficient to treat AK and BD compared to their counterparts ($p=0.020$ and $p=0.048$ respectively). Complete results are presented in Supplemental Table S1.

The treatment option known by most NHPs in general was surgical excision (93.9%), followed by cryotherapy (81.8%), topical 5-fluorouracil (71.2%), radiotherapy (48.7%),

photodynamic therapy (26.8%) and topical imiquimod (20.2%). A complete overview of the different treatment options in (pre)malignant skin lesions is provided in Table 3. More experienced NHPs and NHPs who followed CME concerning (pre)malignant skin lesions were more often familiar with topical 5-fluorouracil ($p<0.01$ and $p=0.015$, respectively) and radiotherapy ($p=0.027$ and $p<0.01$, respectively) compared to their colleagues. However, photodynamic therapy was more often known by the less experienced NHPs compared to their colleagues with more years of experience ($p<0.01$). An overview of these data is presented in Supplemental Table S2. Seven respondents (2.0%) were not familiar with any of the above-mentioned treatment options at all.

Only a limited number of NHPs had used one or more of the above-mentioned treatment options in the past on their own initiative (37.8%) or after consultation of a dermatologist (57.6%). More experienced NHPs were more likely to have performed treatment with topical 5-fluorouracil on their own initiative ($p<0.01$) or after consultation of a dermatologist ($p<0.01$) compared to their less experienced colleagues. Respondents who followed CME concerning (pre)malignant skin lesions more often performed treatment with topical 5-fluorouracil and surgical excision on their own initiative ($p=0.019$ and $p<0.01$, respectively) and more often performed treatment with topical 5-fluorouracil after consultation of a dermatologist ($p=0.021$) than respondents who didn't follow CME concerning this subject (Supplemental Table S2). Few of the NHPs (27.7%) had the possibility to ask a colleague to perform one or more treatment options in (pre)malignant skin lesions, which is also further specified in Table 3.

Most respondents thought that treatment by photodynamic therapy (85.0%) and surgical excision (59.1%) should solely be performed by dermatologists. In contrast, few NHPs answered that cryotherapy (19.6%), topical 5-fluorouracil or imiquimod (both 26.5%) should be exclusive treatment options for dermatologists.

Table 2 Knowledge and skills in diagnosis and treatment of different subtypes of (pre)malignant skin lesions by nursing home physicians (n=347)

	AK	BD	BCC	SCC	M
Sufficient to diagnose, n (%)	284 (81.8)	63 (18.2)	271 (78.1)	185 (53.3)	189 (54.5)
Sufficient to perform treatment, n (%)	172 (49.6)	20 (5.8)	42 (12.1)	14 (4.0)	5 (1.4)
More education requested, n (%)	158 (51.8)	264 (86.2)	193 (63.3)	247 (81.0)	237 (77.7)
Willing to perform (more) treatment after (more) education, n (%)	206 (59.4)	104 (30.0)	107 (30.8)	64 (18.4)	22 (6.3)

Abbreviations: AK, actinic keratosis; BCC, basal cell carcinoma; BD, Bowen's disease; M, melanoma; SCC, squamous cell carcinoma.
Values may not add up due to missing values and rounding.

Table 3 Knowledge and experience of nursing home physicians (n=347) regarding different treatment options in (pre)malignant skin lesions

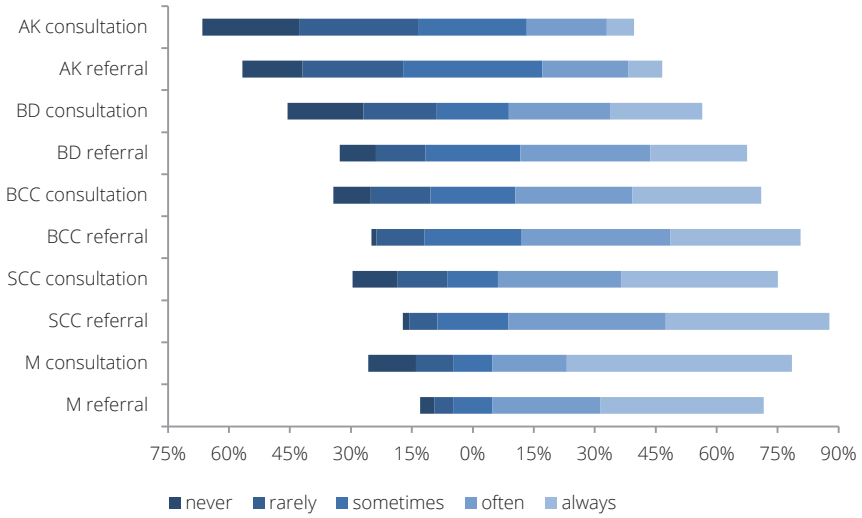
	CRYO	SUR[a]	RT	5FU	IMI	PDT
Knows treatment option, n (%)	284 (81.8)	326 (93.9)	169 (48.7)	247 (71.2)	70 (20.2)	93 (26.8)
Used on own initiative, n (%)	71 (20.5)	48 (13.8)	NA	59 (17.0)	5 (1.4)	0 (0)
Used after consultation of a dermatologist, n (%)	41 (11.8)	32 (9.2)	NA	165 (47.6)	33 (9.5)	4 (1.2)
Could ask a colleague to perform, n (%)	41 (11.8)	63 (18.2)	NA	43 (12.4)	19 (5.5)	3 (0.9)
Willing to perform (more) treatment after (more) education, n (%)	166 (47.8)	115 (33.1)	NA	151 (43.5)	132 (38.0)	39 (11.2)
Should be solely performed by dermatologist, n (%)	68 (19.6)	205 (59.1)	NA	92 (26.5)	92 (26.5)	295 (85.0)

Abbreviations: 5FU, topical 5-fluorouracil; CRYO, cryotherapy; IMI, topical imiquimod; NA, not applicable; PDT, photodynamic therapy; RT, radiotherapy; SUR, surgery.
[a] Including curettage/shave and/or electrodessication. Values may not add up due to missing values and rounding.

Collaboration with dermatologists

Data about the number of NHPs consulting a dermatologist or referring to a dermatologist in different subtypes of (pre)malignant skin lesions in nursing home patients are shown in Figure 1.

Figure 1 The proportions of nursing home physicians consulting a dermatologist or referring to a dermatologist in different subtypes of (pre)malignant skin lesions in nursing home patients



Abbreviations: AK, actinic keratosis; BCC, basal cell carcinoma; BD, Bowen's disease; M, melanoma; SCC, squamous cell carcinoma.

Education

Focusing on education, 105 NHPs (30.3%) followed some form of CME concerning (pre)malignant skin lesions. Years of experience did not have a statistically significant influence on these results. Furthermore, 305 (87.9%) NHPs would like to receive (more) education about one or more subtypes of (pre)malignant skin lesions. The subtype requested the most by these NHPs was BD (86.2%), followed by SCC (81.0%) and melanoma (77.7%). A complete overview is given in Table 2.

The vast majority of the responding NHPs (94.5%) is willing to perform more treatment of (pre)malignant skin lesions themselves after (more) education and the possibility to gain

more experience. An overview by subtype and by treatment option is presented in Table 2 and 3 respectively. Approximately one out of twenty respondents (5.5%) are not willing to perform more treatment in (pre)malignant skin lesions.

Recommendations for improvement

Among the respondent NHPs, 139 (40.1%) had a total of 193 suggestions to improve skin cancer care within the nursing home population. The most frequently given suggestions were: more visits of dermatologists to nursing homes when indicated (25.4%), improving education of physicians involved (20.7%), and more frequent and/or better usage of telemedicine applications (11.9%).

Discussion

We present the results of the first study to investigate skin cancer care among institutionalized older adults. The current role of NHPs in the diagnosis and treatment of different (pre)malignant skin lesions among institutionalized older adults living in nursing homes across the Netherlands seems to be limited, especially when considering the relatively high incidence rates of (pre)malignant skin lesions in this age group. Possible explanations are a lack of knowledge and/or experience, but also logistical issues could be of influence. Furthermore, the possibility to ask a more experienced colleague seems to be another limiting factor.

The willingness of NHPs to perform more skin cancer care themselves seems to be variable, depending on the type of (pre)malignant skin lesion and the type of treatment. To improve the level of knowledge and experience proper education is considered to be of great importance. In addition, this study shows that NHPs who followed CME concerning (pre)malignant skin lesions more often consider their knowledge sufficient to diagnose and treat several types of (pre)malignant skin lesions themselves and were also more often experienced using some treatment modalities themselves. However, next to proper education using the acquired skills in daily practice on a regular basis seems to be important as well to maintain a certain level of knowledge and experience. Subspecialty training of NHPs with special interest in dermatology may contribute to the development and maintenance of skills in daily practice.

Finally, this study shows that a major role in skin cancer care among institutionalized older adults is still reserved for dermatologists, both directly (during an outpatient visit or a visit to a nursing home) as well as indirectly (long distance consultation of a dermatologist, for

instance using a telemedicine application). Therefore it is of importance to have a low threshold and a proper logistic possibility to consult a dermatologist.

Moreover, we believe collaboration between NHPs and dermatologists is essential to improve the level of skin cancer care, because this multidisciplinary approach:

(1) May contribute to overcome possible complicating factors within this population (i.e. multimorbidity, limited life expectancy, cognitive impairment, impossibility to visit a hospital);

(2) May help choosing the most appropriate care from an individualized, patient-centered, and holistic point of view, and;

(3) May be of significant educational value to both NHPs and dermatologists.

It would be interesting to study these benefits of multidisciplinary care in more detail in the future.

Limitations

Possible limitations in this study are the self-administered character of the questionnaire used and the possible influence of more familiarity with the subject of responders compared to non-responders on the results.

Conclusion

The current role of nursing home physicians in skin cancer care in institutionalized older adults seems to be limited, depending on the subtype of (pre)malignant skin lesion and the type of treatment. More education and more consultation of dermatologists (both directly on location within a nursing home, as indirectly for instance by telemedicine applications) is expected to improve skin cancer care in institutionalized older adults.

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Supplemental Table S1 Influence of years of experience (<10 years or ≥ 10 years) and continuing medical education concerning (pre)malignant skin lesions in de past (yes or no) on knowledge and skills in diagnosis and treatment of different subtypes of (pre)malignant skin lesions by nursing home physicians (n=347)[a]

Lesion subtype	Sufficient to diagnose, n (%)					
	<10 YoE	*≥10 YoE*	*P-value*	*No CME*	*CME*	*P-value*
AK	130 (83.9)	153 (80.5)	0.42	196 (81.0)	88 (83.8)	0.53
BD	26 (16.8)	36 (18.9)	0.60	35 (14.5)	28 (26.7)	**<0.01***
BCC	115 (74.2)	154 (81.1)	0.13	181 (74.8)	90 (85.7)	**0.024***
SCC	80 (51.6)	104 (54.7)	0.56	119 (49.2)	66 (62.9)	**0.019***
M	93 (60.0)	96 (50.5)	0.079	123 (50.8)	66 (62.9)	**0.039***
	Sufficient to perform treatment, n (%)					
	<10 YoE	*≥10 YoE*	*P-value*	*No CME*	*CME*	*P-value*
AK	84 (54.2)	87 (45.8)	0.12	110 (45.5)	62 (59.0)	**0.020***
BD	11 (7.1)	9 (4.7)	0.35	10 (4.1)	10 (9.5)	**0.048***
BCC	23 (14.8)	19 (10.0)	0.17	27 (11.2)	15 (14.3)	0.41
SCC	7 (4.5)	7 (3.7)	0.70	8 (3.3)	6 (5.7)	0.30
M	2 (1.3)	3 (1.6)	0.82	3 (1.2)	2 (1.9)	0.63

Abbreviations: AK, actinic keratosis; BCC, basal cell carcinoma; BD, Bowen's disease; CME, continuing medical education; M, melanoma; SCC, squamous cell carcinoma; YoE, years of experience. p<0.05; [a] Numbers per subgroup: <10 YoE (n=155), ≥10 YoE (n=190), No CME (n=242), CME (n=105). Values may not add up due to missings.*

Supplemental Table S2 Influence of years of experience (<10 years or ≥ 10 years) and continuing medical education in de past (yes or no) on knowledge and experience of nursing home physicians (n=347) regarding different treatment options in (pre)malignant skin lesions[a]

Treatment option	*<10 YoE*	*≥10 YoE*	*P-value*	*No CME*	*CME*	*P-value*
CRYO						
Knows treatment option, n (%)	128 (83.7)	154 (81.5)	0.60	197 (82.1)	87 (83.7)	0.72
Used on own initiative, n (%)	38 (25.2)	32 (17.1)	0.069	48 (20.1)	23 (22.8)	0.58
Used after consultation of a dermatologist, n (%)	17 (11.3)	23 (12.4)	0.74	28 (11.8)	13 (12.9)	0.79
SUR[b]						
Knows treatment option, n (%)	148 (96.7)	176 (93.1)	0.14	225 (93.8)	101 (97.1)	0.20
Used on own initiative, n (%)	20 (13.2)	27 (14.4)	0.75	24 (10.0)	24 (23.8)	**<0.01***
Used after consultation of a dermatologist, n (%)	12 (7.9)	20 (10.8)	0.37	18 (7.6)	14 (13.9)	0.72
RT						
Knows treatment option, n (%)	65 (42.5)	103 (54.5)	**0.027***	106 (44.2)	63 (60.6)	**<0.01***
Used on own initiative, n (%)	NA	NA	NA	NA	NA	NA
Used after consultation of a dermatologist, n (%)	NA	NA	NA	NA	NA	NA
5FU						
Knows treatment option, n (%)	97 (63.4)	149 (78.8)	**<0.01***	163 (67.9)	84 (80.8)	**0.015***
Used on own initiative, n (%)	16 (10.6)	42 (22.5)	**<0.01***	34 (14.2)	25 (24.8)	**0.019***
Used after consultation of a dermatologist, n (%)	52 (34.4)	112 (60.5)	**<0.01***	106 (44.7)	59 (58.4)	**0.021***

Supplemental Table S2 Influence of years of experience (<10 years or ≥ 10 years) and continuing medical education in de past (yes or no) on knowledge and experience of nursing home physicians (n=347) regarding different treatment options in (pre)malignant skin lesions[a] (continued)

Treatment option	*<10 YoE*	*≥10 YoE*	*P-value*	*No CME*	*CME*	*P-value*
IMI						
Knows treatment option, n (%)	35 (22.9)	34 (18.0)	0.26	47 (19.6)	23 (22.1)	0.59
Used on own initiative, n (%)	2 (1.3)	3 (1.6)	0.83	2 (0.8)	3 (3.0)	0.14
Used after consultation of a dermatologist, n (%)	10 (6.6)	22 (11.9)	0.10	24 (10.1)	9 (8.9)	0.73
PDT						
Knows treatment option, n (%)	58 (37.9)	35 (18.5)	**<0.01***	63 (26.2)	30 (28.8)	0.62
Used on own initiative, n (%)	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA
Used after consultation of a dermatologist, n (%)	1 (0.7)	3 (1.6)	0.42	3 (1.3)	1 (1.0)	0.83

*Abbreviations: 5FU, topical 5-fluorouracil; CME, continuing medical education; CRYO, cryotherapy; IMI, topical imiquimod; NA, not applicable; PDT, photodynamic therapy; RT, radiotherapy; SUR, surgery; YoE, years of experience. * p<0.05; [a] numbers per subgroup: <10 YoE (n=153), ≥10 YoE (n=189), No CME (n=240), CME (n=104); [b] Including curettage/shave and/or electrodessication. Values may not add up due to missings and rounding.*

6

The impact of high age and comorbidity on management decisions and guideline-adherence in patients with nonmelanoma skin cancer

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Submitted

Abstract

Background

Appropriate medical decision making in patients with nonmelanoma skin cancer (NMSC; including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)) can be challenging, especially in patients with a limited life expectancy (LE). Treatment should be beneficial for the individual patient and deviation from guideline recommendations might be necessary.

Objective

To determine the influence of age and comorbidity, both factors strongly related to limited LE, on NMSC management in daily clinical practice.

Methods

Retrospective analysis of management decisions and guideline-adherence in NMSC patients from one university medical center providing regional dermato-oncologic care. A logistic regression model was used to study the influence of age (<80 years and ≥80 years) and comorbidity (Charlson comorbidity index; CCI) on these outcomes. Various patient and tumor characteristics were included as potential confounders.

Results

401 patients were included (128 ≥80 years). In patients with BCC Mohs micrographic surgery was less often performed in patients ≥80 years compared with younger patients (1.1% vs 8.4%; p=0.019), also after correction for previous treatment (p=0.042) and H-zone location (p=0.014). Correction for CCI showed a trend, not reaching statistical significance (p=0.056). Radiotherapy in BCC was more frequently performed in patients ≥80 years (10.3% vs 2.5%; p=0.003), also after consecutive correction for previous treatment (p=0.007), tumor location (p=0.033), and CCI (p=0.011). In SCC no significant treatment differences were found between the age groups. Overall guideline-adherence was high (88%-90%) and guideline-deviation was not influenced by age (OR=0.834; 95%CI 0.508-1.371; p=0.475) or CCI (OR=0.919; 95%CI 0.764-1.106; p=0.373).

Conclusion

In contradiction with our expectations, management in patients with NMSC is not or only minimally influenced by high age and comorbidity. We believe that better integration of aspects related to a limited LE in NMSC management might optimize care and prevent overtreatment. Future research on the general prognostication, prediction of the patient burden caused by tumor and treatment, and time to benefit in NMSC management is strongly recommended.

Introduction

Nonmelanoma skin cancer (NMSC) is the most common cancer worldwide. NMSC includes basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Dermatologists are expected to be more and more confronted with older adults with NMSC, considering (1) the increasing incidence rates of NMSC in general, (2) the rising incidence rates of NMSC with increasing age, (3) and the aging world population.[1,2] In general, the majority of NMSC has a relatively low malignant potential compared to many other cancer types. However, potential morbidity and even mortality should not be underestimated.[1] Adequate medical decision making in patients with NMSC requires physicians to be aware of several important aspects, including patient and tumor characteristics (e.g. tumor subtype, comorbidity, and life expectancy), treatment goals, and the availability of diagnostic and treatment options. Treatment should be beneficial for the individual patient and both the risk of over- and undertreatment should be carefully weighed. Consequently, management decisions in patients with NMSC may be challenging, especially in the growing population of frail older adults with a limited life expectancy (LE).[3,4]

The main purpose of clinical practice guidelines (CPGs) is to assist physicians in medical decision making, based on the best evidence available and thereby optimizing healthcare.[5] However, CPG-recommendations might not be applicable for every individual, and guidance by CPGs in older adult patients and patients with multiple comorbidities was shown to be limited.[6-8] Therefore, properly reasoned deviation from CPG-recommendations may be in the best interest of a patient and should be considered in some situations. Estimating a patient's LE is difficult. Besides age, a patient's LE may be influenced by several factors, of which comorbidity is considered the strongest and best studied predictor.[9-13] It might be expected that a limited LE and influencing factors might contribute to the extent of CPG-deviation in NMSC, but little is known regarding these decisions from daily practice. Hence, the aim of this study was to determine the influence of high age and comorbidity on management in patients with NMSC in daily clinical practice.

Methods

Setting and patient selection

Patients with NMSC seen in the outpatient dermatology department of the Radboud university medical center in Nijmegen, the Netherlands, were retrospectively analyzed. Selection of histological proven BCCs or SCCs diagnosed in 2012 or 2013 took place using

the national pathology database (PALGA) combined with the patient charts. Patients were sorted in two age groups (<80 years or ≥80 years), based on the United Nations age stratification[2] and the Dutch LE data by Statistics Netherlands (mean residual LE of 4.5 years at an age of 80 years).[14,15] Since every lesion suspicious for NMSC is histopathologically confirmed in our hospital, it is assumed that no cases were missed. In case multiple tumors per patient were found, only the first tumor was included. Exclusion criteria were: (1) tumors other than BCC or SCC (including basosquamous carcinoma), (2) non-cutaneous tumors (e.g. mucosal), (3) patients using chronic immunosuppressive medication, (4) patients having a genetic disorder resulting in an increased risk to develop NMSC (e.g. basal cell nevus syndrome, oculocutaneous albinism, and epidermodysplasia verruciformis), (5) clinical trial subjects, and (6) patients in which diagnosis and/or treatment was not performed within our hospital.

Data collection and quality control

Data of all patients included were independently collected by two data-collectors (SL and CM) using a standardized form. Discrepancies were discussed between the two data collectors and in case no consensus could be reached a third author was consulted (RB or MG). A pilot study of 20 patients was initially performed as a data-collection training (to test the standardized form, to discuss doubtful cases, and to increase interobserver agreement). A data-collector manual was created to document all definitions and agreements.

Patient and tumor characteristics

Several patient and tumor characteristics were collected (Table 1). Comorbidity was classified using the Deyo adaptation of the Charlson Comorbidity Index (CCI; ICD-10 version), which is the most commonly used tool to assess comorbidity, validated in several populations. This includes assigning a weighted score to 17 groups of comorbid conditions when present in a patient (resulting in a score ranging from 0-30). Weights are based on their relative risk on 1-year mortality.[12,13,16-18] When tumor characteristics were inconsistently reported, the pathology report after surgical excision overruled the biopsy report.

Management decisions

Data regarding management decisions and guideline-adherence, including reasons for non-adherence, were collected. Guideline-adherence was based on two AUDIT-checklists for BCC and SCC, respectively (Supplemental File S1 and S2). The 16-item checklist for BCC was based on a previously developed and tested checklist.[19] The 21-item checklist used for SCC was newly developed using the same principles as the BCC-checklist. Both checklists included items related to risk factors, diagnosis, staging, treatment, prevention, and follow-up. All included items were directly based on recommendations from the Dutch

guidelines.[20,21] Guideline-adherence was calculated dividing the number of items fulfilled by the total number of items. Only items applicable for that specific patient were included in the calculation (e.g. in case a tumor was solely treated by radiotherapy the items regarding surgical excision were not included).

Statistics

Primary outcome in this study was guideline-adherence (which included data regarding management decisions). Age and comorbidity are the main factors of influence on guideline-adherence studied. Interobserver agreement was measured using Cohen's κ for each relevant variable. Since the amount of missing data was small, no imputation of missing data was performed and only the available data per variable was analyzed. For a detailed description of the univariate and multivariable logistic regression models used in this study see Supplemental File S3. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 22.0 (IBM Corporation, Armonk, NY).

Results

Patient and tumor characteristics

A total of 401 patients were included, of which 128 patients were aged ≥80 years. Interobserver agreement was substantial to excellent for all variables (median, κ=0,971; range, 0.646 to 1.000). All discrepancies could be solved during consensus-meetings between the two data collectors. Comparison between the two age groups showed that more patients within the older age group had a positive history for NMSC and a higher CCI. Furthermore, tumors within the older age group were more often SCC, less often superficial BCC, more often located within the head and neck area and had a larger diameter. A full overview of patient and tumor characteristics is given in Table 1.

Management decisions

Univariate analysis

In both SCC and BCC, conventional surgical excision was the treatment option performed most frequently (Table 2 and 3). Comparison between both age groups in BCC showed that Mohs micrographic surgery (MMS) was performed less often, and radiotherapy (RT) was performed more often in the older age group. In SCC, no differences regarding treatment options were found comparing both age groups.

Table 1 Patient and tumor characteristics

Characteristics	*Overall population (n=401)*	*Patients aged <80 y (n=273)*	*Patients aged ≥80 y (n=128)*	*P-value*
Patient				
Age, median (range), y	71.0 (30-97)	64.0 (30-79)	83.0 (80-97)	**<0.001***
Male sex, n (%)	203 (50.6)	133 (48.7)	70 (54.7)	0.265
Positive history for NMSC, n (%)[a]	222 (55.5)	131 (48.0)	91 (71.7)	**0.001***
CCI, median (range)	1 (0-7)	0 (0-7)	2 (0-7)	**0.001***
Tumor-related complaints[b], n (%):				
Yes	138 (34.4)	96 (35.2)	42 (32.8)	0.897
No	235 (58.6)	158 (57.9)	77 (60.2)	
Unknown	28 (7.0)	19 (7.0)	9 (7.0)	
Tumor				
Histopathological subtype, n (%):				
SCC	75 (18.7)	34 (12.5)	41 (32.0)	**0.001***
Nodular BCC	81 (20.2)	59 (21.6)	22 (17.2)	
Superficial BCC	89 (22.2)	77 (28.2)	12 (9.4)	
Infiltrative BCC	47 (11.7)	30 (11.0)	17 (13.3)	
Micronodular BCC	40 (10.0)	31 (11.4)	9 (7.0)	
Mixed type BCC	69 (17.2)	42 (15.4)	27 (21.1)	

Table 1 Patient and tumor characteristics (continued)

Characteristics	*Overall population (n=401)*	*Patients aged <80 y (n=273)*	*Patients aged ≥80 y (n=128)*	*P-value*
Tumor				
Location, n (%):				
Head and neck area	215 (53.6)	126 (46.2)	89 (69.5)	**0.001***
Trunk	121 (30.2)	101 (37.0)	20 (15.6)	
Upper limbs	27 (6.7)	18 (6.6)	9 (7.0)	
Lower limbs	38 (9.5)	28 (10.3)	10 (7.8)	
High-risk location, n (%):				
H-zone[c]	129 (39.6)	82 (34.3)	47 (54.0)	**0.001***
Lip or ear[d]	4 (5.3)	2 (5.9)	2 (4.9)	1.000
Largest diameter, median (range), in mm[e]	9.0 (2-45)	8.0 (2-30)	10.0 (2-45)	**0.027***
Tumor depth, median (range), in mm[d,f]	2.0 (1-9)	2.0 (1-8)	2.5 (1-9)	0.267
Degree of histological differentiation[d], n (%):				
Well-differentiated	26 (34.7)	17 (50.0)	9 (22.0)	**0.029***
Moderately-differentiated	43 (57.3)	15 (44.1)	28 (68.3)	
Poorly-differentiated	2 (2.7)	0 (0)	2 (4.9)	

Table 1 Patient and tumor characteristics (continued)

Characteristics	*Overall population (n=401)*	*Patients aged <80 y (n=273)*	*Patients aged ≥80 y (n=128)*	*P-value*
Tumor				
Perineural invasion[d,g], n (%)	6 (8.5)	1 (3.2)	5 (12.5)	0.222
Vascular and/or lymphatic invasion[d,g], n (%)	1 (1.4)	0 (0)	1 (2.5)	NA
Previously treated (recurrence), n (%)	24 (6.0)	15 (5.5)	9 (7.0)	0.545
TNM-stage[d,h]:				
Stage I	58 (77.3)	28 (82.4)	30 (73.2)	0.344
Stage II or higher	17 (22.7)	6 (17.6)	11 (26.8)	

Abbreviations: BCC, basal cell carcinoma; CCI, Charlson comorbidity index; NMSC, nonmelanoma skin cancer; SCC, squamous cell carcinoma; y, years.
*[a] 1 missing; [b] Tumor-related complaints mentioned were bleeding, itch, pain and/or ulceration; [c] BCC only; [d] SCC only; [e] 33 missing; [f] 2 missing: [g] 4 missing. [h] Staging based on the classification of the American Joint Commission on Cancer (AJCC) TNM system[26]; * p≤0.05. Values may not add up due to missing data and rounding.*

Table 2 Management decisions and guideline-adherence in squamous cell carcinoma

Characteristics	*Overall population (n=75)*	*Patients aged <80 y (n=34)*	*Patients aged ≥80 y (n=41)*	*P-value*
Treatment performed, n (%):				
Conventional SE	72 (96.0)	33 (97.1)	39 (95.1)	1.000
RT	3 (4.0)	2 (4.9)	1 (2.9)	
Compliance (guideline-adherence ≥90%), n (%)	23 (30.7)	12 (35.3%)	11 (26.8%)	0.429
Guideline-adherence, median (range), in %	88 (56-100)	87 (63-100)	88 (56-100)	0.898
Guideline-adherence, per recommendation, n (%):				
Prevention and risk factor evaluation:				
Advice on appropriate sun protection	47 (62.7)	21 (61.8)	26 (63.4)	0.883
Evaluation of risk factors[a]	45 (60.0)	19 (55.9)	26 (63.4)	0.507
Diagnosis / staging:				
Palpation regional lymph nodes performed	53 (70.7)	25 (73.5)	28 (68.3)	0.620
Histological confirmation by skin biopsy	74 (98.7)	33 (97.1)	41 (100)	0.453
Ultrasound of regional lymph nodes in high-risk SCC[b]	8 (47.1)	3 (50.0)	5 (45.5)	1.000
Reporting and/or photographing exact location	75 (100)	34 (100)	41 (100)	NA
Primary or recurrent tumor reported	69 (92.0)	30 (88.2)	39 (95.1)	0.401
Maximum tumor diameter reported and adequately included in staging	40 (53.3)	18 (52.9)	22 (53.7)	1.000
Perineural invasion reported and adequately included in staging	70 (93.3)	31 (91.2)	39 (95.1)	0.654
Vascular invasion reported and adequately included in staging	70 (93.3)	31 (91.2)	39 (95.1)	0.654

Table 2 Management decisions and guideline-adherence in squamous cell carcinoma (continued)

Characteristics	*Overall population (n=75)*	*Patients aged <80 y (n=34)*	*Patients aged ≥80 y (n=41)*	*P-value*
Diagnosis/staging (continued):				
Histological differentiation reported and adequately included in staging	75 (100)	34 (100)	41 (100)	NA
Tumor depth reported and adequately included in staging	71 (94.7)	31 (91.2)	40 (97.6)	0.323
Treatment:				
Using 5 mm excision margin when recommended	50 (100)	25 (100)	25 (100)	NA
Using 10 mm excision margin when recommended	1 (12.5)	0 (0)	1 (14.3)	NA
Re-excision in high-risk SCC[b] with <2 mm tumor-free margin	4 (50.0)	2 (100)	2 (33.3)	0.429
Reason for choosing other suitable treatment option reported	6 (100)	2 (100)	4 (100)	NA
Did not perform treatment option which is discouraged in guideline	75 (100)	34 (100)	41 (100)	NA
Follow-up:				
At least 6-monthly follow-up during the first year for low-risk SCC	49 (89.1)	24 (96.0)	25 (83.3)	0.204
At least 3-monthly follow-up during the first year for high-risk SCC[b]	9 (69.2)	5 (100)	4 (50.0)	0.105
Follow-up examination at least included inspection and palpation of treated area and regional lymph nodes, together with total-body skin examination	59 (100)	29 (100)	30 (100)	1.000
Primary care physician is informed about diagnosis and management	62 (82.7)	27 (79.4)	35 (85.4)	0.498

Abbreviations: NA, not applicable; RT, radiotherapy; SCC, squamous cell carcinoma; SE, surgical excision; y, years. [a] Sun exposure behavior, medical history (including history of skin cancer), current medication and smoking should have at least been included in the evaluation of risk factors; [b] High-risk SCC defined as T2 or higher according to the classification of the American Joint Commission on Cancer (AJCC) TNM system.[26] Values may not add up due to missing data and rounding.

Table 3 Management decisions and guideline-adherence in basal cell carcinoma

Characteristics	*Overall population (n=326)*	*Patients aged <80 y (n=239)*	*Patients aged ≥80 y (n=87)*	*P-value*
Treatment performed, n (%)[a]:				
Conventional SE	237 (72.7)	172 (72.0)	65 (74.7)	**0.004***
PDT	34 (10.4)	25 (10.5)	9 (10.3)	
IMI	17 (5.2)	15 (6.3)	2 (2.3)	
MMS	21 (6.4)	20 (8.4)	1 (1.1)	
RT	15 (4.6)	6 (2.5)	9 (10.3)	
No treatment	2 (0.6)	1 (0.4)[b]	1 (1.1)[c]	
Compliance (guideline-adherence ≥90%), n (%)	178 (54.6)	134 (56.1)	44 (50.6)	0.378
Guideline-adherence, median (range), in %	90 (44-100)	90 (50-100)	90 (44-100)	0.301
Guideline-adherence, per recommendation, n (%):				
Prevention:				
Advice on appropriate sun protection	230 (70.6)	185 (77.4)	45 (51.7)	**<0.001***
Diagnosis:				
Histological confirmation by skin biopsy	323 (99.1)	236 (98.7)	87 (100)	0.568
Histopathological subtype reported	326 (100)	239 (100)	87 (100)	NA
Reporting and/or photographing exact location	326 (100)	239 (100)	87 (100)	NA
Primary or recurrent tumor reported	293 (89.9)	212 (88.7)	81 (93.1)	0.244
Maximum tumor diameter reported	160 (49.1)	116 (48.5)	44 (50.6)	0.745

Table 3 Management decisions and guideline-adherence in basal cell carcinoma (continued)

Characteristics	*Overall population (n=326)*	*Patients aged <80 y (n=239)*	*Patients aged ≥80 y (n=87)*	*P-value*
Treatment[a]:				
Using 3 mm excision margin when recommended	90 (97.8)	76 (98.7)	14 (93.3)	0.301
Using 5 mm excision margin when recommended	117 (90.0)	80 (88.9)	37 (92.5)	0.753
Using PDT only in primary, superficial BCC	30 (88.2)	22 (88.0)	8 (88.9)	1.000
Using IMI only in superficial BCC <20 mm and outside of the H-zone	12 (70.6)	11 (73.3)	1 (50.0)	0.515
Reason for choosing other treatment option reported	35 (94.6)	26 (96.3)	9 (90.0)	0.473
Follow-up				
At least yearly follow-up for high-risk and/or multiple BCCs	205 (91.9)	143 (90.5)	62 (95.4)	0.224
Follow-up examination at least included inspection of treated area and sun-exposed skin	204 (99.5)	142 (99.3)	62 (100.0)	1.000
Primary care physician is informed about diagnosis and management	293 (89.9)	209 (87.4)	84 (96.6)	**0.016***

Abbreviations: BCC, basal cell carcinoma; IMI, topical imiquimod; MMC, Mohs micrographic surgery; NA, not applicable; SE, surgical excision; PDT, photodynamic therapy; RT, radiotherapy; y, years. [a] *Data regarding cryosurgery and curettage and cautery were not shown since these treatment options were not performed among the patients within this study;* [b] *Since no clinical tumor residu was seen after punch biopsy a wait-and-see policy was chosen;* [c]*: Patient died before treatment; * p≤0.05.*
Values may not add up due to missing data and rounding.

Table 4 Multiple logistic regression model on the correlation of different factors with guideline-adherence of at least 90% as dependent variable

Variables	*Odds ratio*	*95% CI*	*P-value*
Age (<80 y vs. ≥80 y)	0.834	0.508-1.371	0.475
Charlson comorbidity index (0-30)	0.919	0.764-1.106	0.373
Previous treatment (yes vs. no)	0.608	0.241-1.536	0.293
Treatment method			0.754
Conventional SE	Reference		
PDT	0.985	0.371-2.616	0.976
IMI	0.558	0.164-1.902	0.351
MMS	2.020	0.669-6.094	0.212
RT	1.085	0.381-3.095	0.878
Other	0.867	0.049-15.208	0.922
Tumor type			**0.026***
SCC	Reference		
Nodular BCC	1.950	0.878-4.331	0.101
Superficial BCC	5.309	2.042-13.804	**0.001***
Infiltrative BCC	1.875	0.791-4.448	0.154
Micronodular BCC	1.419	0.577-3.489	0.445
Mixed type BCC	1.540	0.710-3.342	0.274
Location			0.227
Head and neck area	Reference		
Trunk	0.684	0.350-1.336	0.266
Upper limbs	0.563	0.215-1.477	0.243
Lower limbs	0.397	0.160-0.984	**0.046***
Location (high- vs. low-risk)[a]	1.402	0.728-2.700	0.312
Complaints			0.280
No	Reference		
Yes	1.449	0.915-2.294	0.114
Unknown	1.045	0.452-2.419	0.918

Abbreviations: 95% CI, 95% confidence interval; BCC, basal cell carcinoma; IMI, topical imiquimod; MMC, Mohs micrographic surgery; SCC, squamous cell carcinoma; SE, surgical excision; PDT, photodynamic therapy; RT, radiotherapy; y, years. [a] *A BCC located in the H-zone or a SCC located on an ear or lip; * p≤0.05.*

Multivariate analyses

Secondary multivariate logistic regression analyses were performed to study the management differences found in the univariate analysis in more detail. As the number of treatments with MMS and RT were performed in BCC was rather small (21 and 15 times, respectively), a large logistic regression model was not possible. Hence, three consecutive analyses were performed for each treatment option, each with age and one important confounder (location, previous treatment, and CCI, respectively). Inclusion of BCC subtype in the model was not possible due to (1) the relatively low number of BCC treated by MMS and RT, and (2) the extent of variance found in different BCC subtypes treated by both treatment options. MMS was less often performed in BCC in the older age group compared with the younger patients (1.1% vs 8.4%; p=0.019). This finding persisted after consecutive correction for previous treatment (primary vs. recurrent BCC (p=0.042) and location (within or without the H-zone; p=0.014). After correction for CCI the model failed to show a statistical significant difference of treatment of BCC by MMS between the two age groups, although a trend could be seen (p=0.056). The opposite was observed for RT in BCC, which was more frequently performed in the older patient group compared to the younger (10.3% vs 2.5%; p=0.003), also after consecutive correction for previous treatment (p=0.007), location (p=0.033), and CCI (p=0.011).

Guideline-adherence

Univariate analyses

Overall guideline-adherence was high (88% vs. 90% for SCC and BCC, respectively) and did not differ between the two age groups (p=0.898 and p=0.301, respectively). When focusing more specifically on the individual guideline-recommendations advice on appropriate sun protection was less frequently provided in the older age group with BCC (77.4% vs. 51.7%, p<0.001), while the primary care physician was more frequently informed about the diagnosis and management in the older age group with BCC (87.4% vs. 96.6%, p=0.016). All other guideline-recommendations showed no difference in adherence between both age groups. In 4.5% (n=25) of the deviations from guideline recommendations, the reason was extractable from the patient chart. The most frequently mentioned reasons for guideline-deviation were: (1) a limited LE, (2) severe impaired mobility, and (3) a patient's refusal.

Multivariate analyses

Guideline adherence below 90% was considered as "low" guideline-adherence (cut-off based on approximate median). The multiple logistic regression model for this dependent variable is presented in Table 4. The results of this model show that guideline-adherence is not influenced by age (OR=0.834; 95%CI 0.508-1.371; p=0.475) or comorbidity (OR=0.919; 95%CI 0.764-1.106; p=0.373), after correction for the other variables. Of the other variables

in the model, the effect of tumor type is by far the most clear (p=0.026). A much better guideline-adherence in patients with a superficial BCC as opposed to patients with a SCC (OR=5.309; 95%CI 2.042-13.804; p=0.001) was noted.

Discussion

The results in the present study show that management decisions in BCC are influenced by high age to some extent, while the influence of comorbidity seems only minimal to absent. Furthermore, high age and comorbidity did not have a significant influence on management decisions in SCC, or on overall guideline-adherence in both BCC and SCC. The possibility to draw direct conclusions from the results found in this study with respect to quality of care is limited and the definition of optimal skin cancer care remains open for discussion. However, one might expect deviation from regular treatment protocols and guideline recommendations in NMSC to be more common among frail older adults with a limited LE, which was not shown by the results in this study.

Former studies on the impact of high age and comorbidity on treatment decisions in NMSC patients are scarce. Two studies from the United States showed that a limited LE did not influence treatment decisions in patients with NMSC, including treatment with MMS.[22,23] These studies show important agreement with our findings that high age and comorbidity do not have a significant influence on treatment choice in SCC and the decision not to treat NMSC is rare. On the other hand, our finding that MMS is less frequently performed in patients ≥80 years with BCC, while RT is more frequently used in this population, seems to contradict these studies, which might be explained by intercountry differences in healthcare systems and guidelines.

It should be pointed out that medical decision making solely based on age might be a pitfall, since age alone is just one factor influencing life expectancy and the population of older adults is heterogeneous. For instance, on the one hand MMS is a treatment option which might lead to a significant patient burden and overtreatment in some (frail) older patients, especially in case a patient will not live long enough to benefit from this treatment (*time to benefit principle*).[22,23] On the other hand, MMS is a suitable treatment option in some (less frail) older adults and exclusion solely based on age seems to be an insufficient selection method.[24] We believe (more extensive) inclusion of patient characteristics related to frailty and a limited LE in medical decision making in older adults optimizes NMSC care. Examples of these characteristics are: comorbidity, cognition, and functional status. Clinicians may be stimulated to act on this to a greater extent through education, more cooperation with

elderly care specialists, and further inclusion of these considerations within clinical practice guidelines.[8] Furthermore, we believe *watchful waiting* is a suitable alternative for treatment in some patients with an asymptomatic low-risk NMSC, which should be considered more frequently in patients with a limited LE. Instruments to determine (the extent of) frailty and a patient's general prognosis can assist in these management decisions, however currently these are not validated for NMSC patients.[25] Consequently, since reliable and validated methods for general prognostication, prediction of the patient burden caused by tumor and treatment, and *time to benefit* data are lacking in current NMSC literature, management decisions in daily practice might remain complex. We strongly recommend to focus future research on these aspects in order to provide guidance for clinicians.

Limitations

Generalization of the results in this single-center study from one university hospital in the Netherlands should be performed with care, since population and management differences can exist between different healthcare institutions and countries. Since patient records were retrospectively studied non-reporting bias might have occurred, which could have influenced guideline-adherence data. However, it is unlikely this potential non-reporting bias differed among the compared patient groups and therefore its influence on the main outcomes in this study is expected to be limited.

Conclusion

In contradiction with our expectations, the present study shows that management in patients with NMSC is not or only minimally influenced by high age and comorbidity. We believe that better integration of aspects related to a limited LE in NMSC management might optimize care and prevent overtreatment. Future research on general prognostication, prediction of the patient burden caused by tumor and treatment, and time-to-benefit in NMSC management is strongly recommended.

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Supplemental File S1 Checklist on guideline-adherence in patients with squamous cell carcinoma (SCC)

Based on the clinical practice guideline "Squamous cell carcinoma of the skin" of the Dutch Society of Dermatology and Venereology.[1]

PREVENTION:

1. The patient received advice on appropriate sun protective behavior:
☐ Yes
☐ No
Comment:

2. Risk factors to develop squamous cell carcinoma were adequately evaluated:
☐ Yes
☐ No
Comment:

DIAGNOSIS / STAGING:

3. Regional lymph nodes were palpated before therapy was started:
☐ Yes
☐ No
Comment:

4. A punch biopsy of the SCC was performed before therapy was started:
☐ Yes
☐ No
Comment:

5. An ultrasound (including biopsy in case of a suspicion of a lymph node metastasis) of regional lymph nodes was performed in high-risk SCC[a]:
☐ Yes
☐ No
☐ Not applicable
Comment:

6. The exact location of the SCC was reported and/or photographed:
☐ Yes
☐ No
Comment:

7. It was documented if the SCC was previously treated:
☐ Yes
☐ No
Comment:

8. The maximum tumor diameter was reported and adequately included in staging:
☐ Yes
☐ No
Comment:

9. Pathologic assessment on perineural invasion was reported and adequately included in staging:
☐ Yes
☐ No
Comment:

10. Pathologic assessment on vascular invasion was reported and adequately included in staging:
☐ Yes
☐ No
Comment:

11. Pathologic assessment on histological differentation was reported and adequately included in staging:
☐ Yes
☐ No
Comment:

12. Pathologic assessment on depth of tumor growth was reported and adequately included in staging:
☐ Yes
☐ No
Comment:

TREATMENT:
Conventional surgical excision:
13. An excision margin of 5 mm was used when recommended (in case of primary and low-risk SCC[a]):
☐ Yes
☐ No
☐ Not applicable
Comment:

14. An excision margin of 10 mm was used when recommended (in case of recurrent and/or high-risk SCC[a]):
☐ Yes
☐ No
☐ Not applicable
Comment:

15. Re-excision was performed in case of a high-risk SCC[a] with <2 mm tumor-free margin:
☐ Yes
☐ No
☐ Not applicable
Comment:

Other treatment options:
16. The reason(s) to choose for another suitable treatment option (e.g. radiotherapy, cryosurgery, or curettage and cautery) are well-documented:
☐ Yes
☐ No
☐ Not applicable
Comment:

17. Treatment options discouraged by the guideline (e.g. topical imiquimod, intralesional interferon alfa, of photodynamic therapy) were not performed:
☐ Yes
☐ No
Comment:

FOLLOW-UP:
18. A follow-up examination was performed at least 6-monthly during the first year after treatment in case of a low-risk SCC[a]:
☐ Yes
☐ No
☐ Not applicable
☐ Unknown
Comment:

19. A follow-up examination was performed at least 3-monthly during the first year after treatment in case of a high-risk SCC[a]:
☐ Yes
☐ No
☐ Not applicable
☐ Unknown
Comment:

20. Follow-up examination at least included inspection and palpation of the treated area, palpation of the regional lymph nodes and total-body examination:
☐ Yes
☐ No
☐ Unknown
Comment:

21. The primary care physician (general practitioner or elderly care physician) of the patient was informed about the diagnosis and therapy of the SCC:
☐ Yes
☐ No
Comment:

[a] High-risk SCC defined as T2 or higher according to the classification of the American Joint Commission on Cancer (AJCC) TNM system.[2]

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Supplemental File S2 Checklist on guideline-adherence in patients with basal cell carcinoma (BCC)

Based on previously developed and tested AUDIT-checklist,[1] originally based on the clinical practice guideline "Evidence-based guideline on the treatment of basal cell carcinoma" of the Dutch Society of Dermatology and Venereology.[2]

PREVENTION:

1. The patient received advice on appropriate sun protective behavior:
☐ Yes
☐ No
Comment:

DIAGNOSIS:

2. A punch biopsy of the BCC was performed before therapy was started:
☐ Yes
☐ No
Comment:

3. The histopathological subtype of the BCC was reported:
☐ Yes
☐ No
Comment:

4. The exact location of the BCC was reported and/or photographed:
☐ Yes
☐ No
Comment:

5. It was documented if the BCC was previously treated:
☐ Yes
☐ No
Comment:

6. The maximum tumor diameter was reported:
☐ Yes
☐ No
Comment:

TREATMENT:

Conventional surgical excision:

7. An excision margin of 3 mm was used when recommended (in case of a non-infiltrative and primary BCC with a maximum diameter ≤10 mm):

☐ Yes
☐ No
☐ Not applicable
Comment:

8. An excision margin of 5 mm was used when recommended (in case of an infiltrative and/or recurrent BCC with a maximum diameter >10 mm):

☐ Yes
☐ No
☐ Not applicable
Comment:

Photodynamic therapy:

9. Only performed in a primary, superficial BCC:

☐ Yes
☐ No
☐ Not applicable
Comment:

Cryosurgery:

10. Only performed in a superficial or nodular BCC with a maximum diameter ≤20 mm:

☐ Yes
☐ No
☐ Not applicable
Comment:

Topical imiquimod:

11. Only performed in a primary and superficial BCC with a maximum diameter ≤20 mm and outside of the H-zone:

☐ Yes
☐ No
☐ Not applicable
Comment:

Curettage and cautery:

12. Only performed in a primary, superficial or nodular BCC with a maximum diameter ≤5 mm and outside of the H-zone:

☐ Yes
☐ No
☐ Not applicable
Comment:

Other treatment options (e.g. radiotherapy, Mohs micrographic surgery):

13. The reason(s) to choose for another treatment option are well-documented:

☐ Yes
☐ No
☐ Not applicable
Comment:

FOLLOW-UP:

14. A follow-up examination was performed at least within one year after treatment in case of a high-risk BCC and/or in case of multiple BCC:

☐ Yes
☐ No
☐ Not applicable
☐ Unknown
Comment:

15. Follow-up examination at least included inspection of the treated area and the sunexposed skin:

☐ Yes
☐ No
☐ Not applicable
☐ Unknown
Comment:

16. The primary care physician (general practitioner or elderly care physician) of the patient was informed about the diagnosis and therapy of the BCC:

☐ Yes
☐ No
Comment:

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Supplemental File S3 Details of the regression models on the correlation of different factors with guideline-adherence used in this study

First, a descriptive, univariate analysis was performed. Categorical variables were expressed as numbers (and proportions) and compared using a Chi-squared test or Fisher's exact test when appropriate. Numerical variables were expressed as medians with ranges, and compared using a Mann-Whitney test.

Since the distribution of guideline-adherence was expected to be very skew and since the relation of age and comorbidity with guideline-adherence is likely to be confounded by various patient- and tumor characteristics (Table 4), a multivariable logistic regression analysis was performed afterwards.

As no well established cut-off for a satisfactory level of guideline-adherence is known from literature, a cut-off close to the median was selected and two categories were formed ("high" vs "low" guideline-adherence). This would yield two groups of approximately equal size, which maximizes the power of the study. A priori estimates of study precision would require extensive knowledge about the correlation between all variables to be included in the model. That information is not available. Therefore, we applied the rule of thumb that for multivariable logistic regression at least 10 observations per variable in the model are required on the least prevalent of the two outcomes. Therefore, at least 360 (18x10x2) observations were needed in the case guideline-adherence has a 50:50 distribution over "high" vs "low". To allow for an unbalance we decided to aim for inclusion of 400 patients. The distribution with regard to age is not required to be balanced, but a large unbalance would result in a relatively low precision for the effect of age on guideline-adherence. Since it became clear during the study that the consecutive inclusion in the younger group was much faster than in the old group, after the inclusion of 336 patients (274 aged <80 years; 62 aged ≥80 years), we continued by only including patients from the older age group. In addition, secondary multivariate logistic regression analyses were performed to study differences in management decisions found in the univariate analyses in more detail.

7

The epidemiology and clinicopathological features of basal cell carcinoma in patients aged 80 years and older: a systematic review

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Abstract

Importance

The number of oldest-old (persons aged ≥80 years) is rapidly growing worldwide. Basal cell carcinoma (BCC) are common in this age group and the management could be challenging in this population.

Objective

Obtaining an overview of the epidemiology and clinicopathological features of BCC in the oldest-old to guide healthcare providers and policy makers.

Evidence review

A systematic review of literature was performed using PubMed, Excerpta Medica Database (EMBASE), and the Cochrane Library. Study selection, quality assessment and data extraction was performed by 2 independent reviewers. For quality assessment (including the risk of bias) the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist was used, combined with the Quality Rating Scheme for Studies and Other Evidence. Data were described through a narrative synthesis and tabulation.

Findings

High and increasing incidence rates of BCC in the oldest-old were found ranging from 13 to 12 112 per 100 000 person-years, strongly depending on factors like study population and clinical setting. Basal cell carcinoma in the oldest-old are more common in men, mostly of the nodular subtype, and located within the head and neck region. Interpretation and generalization of the data was limited by the heterogeneity of study populations, methods and outcomes. Data concerning impact on health-related quality of life (HRQoL) and prognostication are scarce.

Conclusions and relevance

The incidence of BCC among the oldest-old is high and increasing. Epidemiologic and clinicopathological data from current literature provide only limited guidance in clinical decision making due to heterogeneity and scarcity. Future research should focus more specifically on BCC in the oldest-old, together with prognostication and their relation with HRQoL in both the short and longer term.

Introduction

A rapid expansion of the oldest-old (persons aged ≥80 years) is currently being seen worldwide, with an expected global increase in this age group from 125 million people in 2015 to 434 million in 2050 (1.7% and 4.5% of the world population, respectively).[1] Basal cell carcinoma (BCC) is a common skin tumor among older adults. Although mortality caused by BCC is exceptional, a considerable morbidity may be caused owing to pain, secondary infection, and disfigurement. Consequently, early detection and treatment of BCC are considered key elements in appropriate skin cancer care. Decisions about what constitutes appropriate medical care in oldest-old patients with BCC is often complicated by several factors, like logistical difficulties, multimorbidity, quality of life dilemmas, and a limited life expectancy. To develop the best possible individualized care for oldest-old patients with BCC, it is important for clinicians and policy makers to have insight into the epidemiological and clinicopathological aspects of BCC in this population. Therefore, the purpose of this systematic review was to obtain an overview of the epidemiology and clinicopathological features of BCC in the oldest-old.

Methods

Search strategy, selection criteria and data collection

Search strategy

A comprehensive literature review was conducted to identify relevant articles containing data about epidemiology and clinicopathological features of BCC in the oldest-old. A search strategy was developed with the support of a medical librarian and performed by 2 independent reviewers (SL and LvV). PubMed, Excerpta Medica Database (EMBASE), and the Cochrane Library were searched for articles published up to July 18, 2015. A detailed overview of the search strategy and strings used is presented in Supplemental Table S1.

Selection criteria

Overall exclusion criteria were the following: full-text not available, non-English/Dutch publications, and conference abstracts. All epidemiologic studies reporting age-specific rates in the oldest-old were included. Incidence rates had to be specifically identifiable and/or sufficient data allowing incidence rate calculation had to be described. In addition, the reviewers could decide to include studies without these strict age-specific rates if they were consensually considered of great value. When multiple studies reported about identical study populations over an identical period of time the data were included only once.

Data collection

Data were gathered using the reference management software EndNote, version X5.0.1 (Thomson Reuters, New York City, USA). When full-text articles were not online-available, a paper copy was tried to obtain in our local medical library, and/or the Dutch Central Catalogue (PiCarta), and/or the first author was tried to contact. Selection of studies for eligibility (by title, abstract and full-text screening respectively) and data extraction using a predefined data sheet were performed by two independent reviewers (SL and LvV). Secondly, inconsistencies were discussed until consensus could be reached. In case no consensus could be reached a third reviewer (MG) was involved. No blinding of the reviewers to the authors names, institutions or journals was performed. In case a study was considered of potential value the first author was contacted to request for additional data or clarification when: (1) no specific stratification of data for BCC, or (2) no age-specific rates were provided or data needed to calculate age-specific rates were incomplete.

Quality assessment of included studies

The included observational studies were independently assessed on 22 criteria for methodological and reporting quality by the 2 reviewers using the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist and the Quality Rating Scheme for Studies and Other Evidence, as proposed before by others.[2,3,4] The assessment of risk of bias in individual studies at both study and outcome level was included within this quality evaluation. Studies were categorized depending on the proportion of STROBE criteria fulfilled (category A-B-C, respectively fulfilling >80%, 50-80%,and <50% of the criteria).

Synthesis of results and reporting

Data were described though a narrative synthesis and tabulation. Results were presented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement on reporting systematic reviews and meta-analyses of epidemiological studies.[5] Since most studies solely presented crude incidence rates (IRs), these were primarily reported. Standardized IRs were reported only when crude IRs were unavailable. Since the highest age category included in both the European standard population as the World standard population is 85 or older the influence of standardization on the comparability of IRs in the population of patients aged 80 years or older seems limited and was not additionally performed.[6] A summary of key findings based on the quality of evidence found is provided. Quality of evidence was rated as previously suggested by Robinson et al.[7]

Results

As shown in the Figure 1, 13 628 studies were initially identified, of which 83 studies were ultimately included. Quality assessment using the STROBE checklist was performed in 76 studies, and resulted in the following classification: category A, 18 (23.7%); category B, 48 (63.2%); and category C, 10 (13.2%). In the remaining 7 studies the STROBE checklist was not considered appropriate owing to the nonobservational design and therefore was not used for quality assessment.

Epidemiology

Incidence

In total, 27 studies were found reporting age-specific incidence rates (IRs) of BCC in the oldest-old, or sufficient data to calculate age-specific IRs (Table 1).[8-34] In most studies (n=19) IRs based on no more than 1 tumor per patient were presented,[8,10,11,13-18,20-23,25-28,30,34] while in some studies (n=4) multiple tumors per patient were included[19,24,31,32] or no coding method was presented (n=4).[9,12,29,33] Crude IRs (based on no more than 1 tumor per patient) ranged from 13 to 12 112 per 100 000 person-years in the oldest-old, strongly influenced by factors such as sex, geographical location, ethnical background, and time period.

Stratification by sex

Higher IRs for males compared with females were shown in most studies, with a male:female ratio ranging from 1.1-4.4:1 (Table 1).[8-12,14,16-29,31-33] Chuang et al.[15] found IRs were 4 times higher among Japanese women aged 85 years or older in Hawaii compared with men. Traditional occupational differences were stated by the authors as a possible explanation.

Comparison with other age groups

Most studies show IRs keep rising with increasing age for both sexes.[9,10,13-15,17,19,22,24-31] However, some studies indicate a rise until the eighth or ninth decade, after which a slight decrease in IRs was seen for 1 or both sexes.[8,11,12,16,18,20,21,32,34] One Jordanian study[23] found highest IRs among women in the seventh decade, while the IRs for men kept increasing with increasing age. The authors considered inadequate sampling and differences in sun exposure as possible explanatory factors.

Figure 1 Study selection in this systematic review

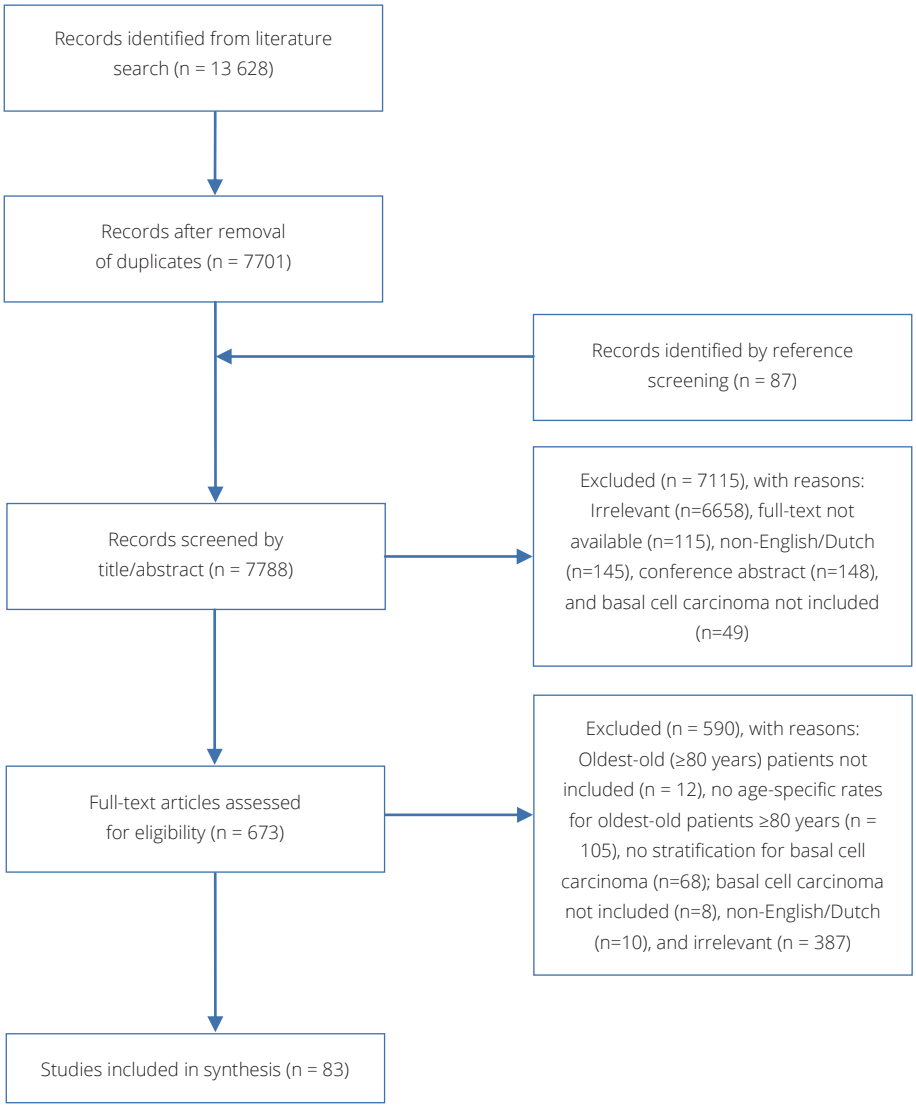

Table 1 Incidence rates of basal cell carcinoma in the oldest-old (patients aged 80 years or older)

Source	Data source	Hist. confir-mation	Coding by[a]	Period	Age-group, y	IRs[b]			M:F ratio	STROBE / QRS
						M	*F*	*Total*		
McKnight, 1979 (Iceland)[8]	Cancer registry	Y	Patient	1955-1974	80-84	75	58	NR	1.3	B / 3
					≥85	13	53		0.2	
Dahl, 1991 (Sweden)[9]	One pathology laboratory	Y	NR	1970-1971	≥80	622	529	NR	1.2	B / 3
				1975-1976		970	562		1.7	
				1980-1981		1126	564		2.0	
				1985-1986		1361	819		1.7	
Levi, 1998 (Switzerland)[10]	Cancer registry	Y	Patient	1974-1994	≥80	550	364	NR	1.5	B / 3
Chuang, 1990 (US)[11]	Local health group database	Y	Patient	1976-1984	≥85	1028	928	950	1.1	B / 3
Magnus, 1993 (Australia)[12]	Cancer registry	Y	NR	1976-1982	80-89	387	293	327	1.3	C / 3
					≥90	325	275	292	1.2	
Kaldor, 1993 (Australia)[13]	Cancer registry	N	Patient	1978-1987	≥80	NR	NR	703	NR	B / 3
Coebergh, 1991 (Netherlands)[14]	Cancer Registry	Y	Patient	1978-1988	80-84	463	344	NR	1.3	B / 3
					≥85	496	384		1.3	
Chuang, 1995 (US)[15]	Prospective physicians registry	Y	Patient	1983-1987	≥85	290	1148	838	0.3	B / 2

Table 1 Incidence rates of basal cell carcinoma in the oldest-old (patients aged 80 years or older) (continued)

Source	Data source	Hist. confir-mation	Coding by[a]	Period	Age-group, y	IRs[b]			M:F ratio	STROBE / QRS
						M	*F*	*Total*		
Reizner, 1993 (US)[16]	Prospective physicians registry	Y	Patient	1983-1987	≥85	3252	3093	3182	1.1	B / 2
Harris, 2001 (US)[17,d]	Cancer registry	Y	Patient	1985-1996	≥80	7550	2898	NR	2.6	B / 3
Holme, 2000 (UK)[18]	Cancer registry	N	Patient	1988	80-84	989	549	684	1.8	A / 3
					≥85	686	895	846	1.6	
				1998	80-84	1188	730	883	0.8	
					≥85	1387	785	927	1.8	
Hoy, 1996 (US)[19,e]	Local health group database	Y	Tumor	1989-1991	≥80	10987	2670	NR	4.1	C / 3
Stang, 2003 (Germany)[20]	Cancer registry	N	Patient	1995-1999	80-84	455	332	NR	1.4	B / 3
					≥85	566	274		2.1	
Bath-Hextall, 2007 (UK)[21]	Primary care database	N	Patient	1996-2003	≥80	742	491	574	1.5	A / 3
Raasch, 2002 (Australia)[22]	Cancer registry	Y	Patient	1997-1999	≥80	12112	5525	NR	2.2	B / 2
Omari, 2004 (Jordan)[23]	Cancer registry	Y	Patient	1997-2001	>80	162	80	121	2.0	B / 3

Table 1 Incidence rates of basal cell carcinoma in the oldest-old (patients aged 80 years or older) (continued)

Source	Data source	Hist. confir-mation	Coding by[a]	Period	Age-group, y	IRs[b]			M:F ratio	STROBE / QRS
						M	*F*	*Total*		
Brougham, 2010 (New Zealand)[24]	Pathology laboratories	Y	Tumor	1997-2007	≥80	3764	1816	2716	2.1	B / 2
Revenga Arranz, 2004 (Spain)[25]	Hospital database	Y	Patient	1998-2000	80-100	909	326	550	2.8	B / 3
Stang, 2007 (Germany)[26]	Prospective physicians registry	NR	Both[f]	1998-2003	≥80	1066[f]	464[f]	NR	2.3	B / 3
Eisemann, 2013 (Germany)[27,g]	Cancer registry	Y	Patient	1998-2000	≥80	703	399	NR	1.8	A / 3
				2008-2010		812	498		1.6	
Asgari, 2015 (US)[28]	Health insurance database	Y	Patient	1998-2012	≥80	4941	2537	3484	1.9	A / 3
Celic, 2009 (Croatia)[29]	Dermatologists survey and cancer registry	Y	NR	2003-2005	≥80	652	327	NR	2.0	B / 3
Musah, 2013 (UK)[30,g]	Primary care database	N	Patient	2004	≥80	NR	NR	660	NR	A / 3
				2005				677		
				2006				716		
				2007				784		
				2008				754		
				2009				744		

Table 1 Incidence rates of basal cell carcinoma in the oldest-old (patients aged 80 years or older) (continued)

Source	Data source	Hist. confir-mation	Coding by[a]	Period	Age-group, y	IRs[b]			M:F ratio	STROBE / QRS
						M	*F*	*Total*		
Musah, 2013 (UK)[30,g] *(cont.)*	Primary care database	N	Patient	2010				718		
De La Torre-Lugo, 2010 (Puerto Rico)[31]	Pathology laboratories	Y	Tumor	2005	≥85	1260	610	860	2.1	B / 3
Bielsa, 2009 (Spain)[32]	Prospective dermatologists registry	N	Tumor	2006-2007	80-84	3444	1523	2197	2.3	B / 3
					≥85	3910	1156	1914	3.4	
Saint-Yves, 1988 (Australia)[33,c]	Cancer registry	Y	NR	1981-1985	80-84	16(W)	9(W)	NR	1.8	B / 3
					≥85	18(W)	14(W)		1.3	
Sella, 2015 (Israel)[34,c]	Health insurance database	Y	Patient	2006-2011	≥80	NR	NR	999(E)	NR	B / 3

Abbreviations: cont, continued; (E), European; F, females; Hist, histological; IRs, incidence rates; M, males; N, no; NR, not reported; QRS, quality rating scheme; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; United Kingdom; US, United States; (W), World; y, years; Y, yes (all cases histologically confirmed). [a] Coding by patient means no more than one tumor per patient was included, coding by tumor means multiple tumors per patient might have been included; [b] IRs are given per 100 000 person-years and reported as crude rates unless otherwise specified; [c] Only standardized IRs available and reported, the population used for standardization given between parentheses (World or European); [d] Age-specific incidence rates only available for the year 1996; [e] Only rates for non-Hispanic whites are shown (rates for Hispanic whites also available but not shown); [f] Rates coded by patient were shown (rates coded by tumor also available but not shown); [g] Additional information was obtained after contact with the first author. STROBE classification based on criteria fulfilled (A: >80%; B: 50-80%; C: <50%); quality rating scheme (1, properly powered and conducted randomized clinical trial; systematic review with meta-analysis; 2, well-designed controlled trial without randomization; prospective comparative cohort trial; 3, case-control studies; retrospective cohort study; 4, case series with or without intervention; cross-sectional study; 5, opinion of respected authorities; case reports).

Time trends

Six studies report age-specific changes of IRs over time, with annual percentage changes (APCs) ranging from -2.2% to 6.4%.[21,24,28,30,35,36] All studies but 1 showed significant increases in APCs over time in the oldest-old. In 1 study from the United Kingdom[21] no significant changes in IRs were found in a primary care database over the period 1996 to 2003 (APC, -2.2%; 99%CI: -4.6 to 0.2). Most studies show lower APCs among the oldest-old compared with younger patients, indicating a relatively faster increasing incidence in younger patients.[21,24,30,35,36] In contrast, 1 study reported highest APCs in patients aged 80 years or older, especially in men.[28]

Prevalence

Point-prevalences of BCC in geriatric populations range broadly (median 0.8%; range, 0% to 21%),[37-59] strongly influenced by the clinical setting (i.e. dermatology outpatient clinic, geriatric ward, nursing home), definition of older adults and population characteristics like size and racial and cultural differences (e.g. over half of the included studies was performed in Asian countries). All studies providing prevalence data of BCC in geriatric populations (regardless of age categories) are summarized in Table 2.

Mortality

Only 2 studies provide specific mortality rates (MRs) for BCC in the oldest-old, reporting crude MRs of 6.49 and 2.88 per 100 000 person-years in people aged 85 years or older in 2 consecutive cohorts of Rhode Island residents.[60,61] Although death owing to BCC is very uncommon, both studies showed that MRs owing to BCC were highest in patients aged 85 years or older compared with younger patients. In general, the potential influence of misclassification of causes of death should always be taken into account in studies reporting MRs.

Multiple basal cell carcinoma

In a meta-analysis published in 2013, a mean 5-year cumulative risk of 36.2% to develop a subsequent BCC after an initial BCC was calculated in patients of all ages combined.[62] Conflicting data were found concerning the relationship between increasing age and the risk of developing a subsequent BCC.[63-70] The proportion of oldest-old developing multiple BCC ranges from 26.3% to 48.8% (Table 3).[63,64,66,70]

Table 2 Prevalence of basal cell carcinoma in geriatric populations

Source	Period	Population size	Setting	Examined by	Histo. confirmation	Age range, y	Prevalence BCC, % (n)[a]	STROBE/QRS
Bilgili, 2012 (Turkey)[37]	2007-2010	5961	2 DOCs	Dermatologist	NR	65-102	0.5 (30)	B / 3
Bradley, 1991 (Australia)[38]	1988-1989	568	PHI	General practitioner	N	65-100	6.0/10.2 (34/58[b])	C / 3
Chan, 2006 (Hong Kong)[39]	2005	257	4 PHI's	NR	N	69-99	0.8 (2)	B / 4
Chopra, 1999 (India)[40]	1996	214	DOC	Dermatologist	NA	60-85	None	C / 3
Darjani, 2013 (Iran)[41]	2010-2011	440	DOC	Dermatologist	Y	NS (all ≥60)	Overall: 8.9 (39) ≥80: 13.0 (6)	B / 3
Kilic, 2007 (Turkey)[42]	2006	300	3 PHI's	Dermatologist	NA	57-104	None	B / 4
Liao, 2001 (Taiwan)[43]	1993-1999	16 924	DOC	Dermatologist	NR	NS (all ≥65)	0.6 (108)	B / 3
Nair, 2013 (India)[44]	2009-2010	457	DOC	Dermatologist	NR	NS (all ≥60)	0.2 (1)	B / 2
Patange, 1995 (India)[45]	NR	200	NR	NR	NA	55-85	None	C / 4

Table 2 Prevalence of basal cell carcinoma in geriatric populations (continued)

Source	Period	Population size	Setting	Examined by	Hist. confirmation	Age range, y	Prevalence BCC, % (n)[a]	STROBE / QRS
Polat, 2009 (Turkey)[46]	2006	209	DOC	Dermatologist	Y	65-91	4.3 (9)	B / 2
Roodsari, 2008 (Iran)[47]	NR	456	12 PHI's	Dermatologist	NR	29-107	0.4 (2)	C / 4
Shah, 2005 (UK)[48]	NR	100	DOC	Dermatologist	NR	66-90	21.0 (21)	B / 4
Smith, 2002 (Australia)[49]	2000	360	PHI	NH physician, podiatrist and nurse	NR	34-103	3.9 (11)	B / 3
Smith, 2002 (Taiwan)[50]	1999-2000	398	11 PHI's	Dermatologist	NR	22-108	0.3 (1)	B / 4
Swetter, 2003 (US)[51]	1997-2000	374	7 DOCs	Dermatologist	N	28-92	Overall: 11.0 (41) ≥80:13.8 (4)	B / 4
Templier, 2015 (France)[52]	2013	204	Hospital-based acute geriatric unit	Dermatologist	Y	NR	4.4 (9)	A / 3
Thapa, 2012 (Nepal)[53]	2010-2011	330	DOC	Dermatologist	NR	60-97	0.3 (1)	B / 3

Table 2 Prevalence of basal cell carcinoma in geriatric populations (continued)

Source	Period	Population size	Setting	Examined by	Hist. confirmation	Age range, years	Prevalence BCC, % (n)[a]	STROBE / QRS
Tseng, 2015 (Taiwan)[54]	2011	337	PHI	Dermatologist	Y	46-99	1.2 (4)	B / 2
Verbov, 1975 (UK)[55]	1975	170	DOC and inpatients from two hospitals	Dermatologist	NR	60-90	8.2 (14)	C / 2
Weismann, 1980 (Denmark)[56]	1976	584	Multiple PHI (unknown number)	Dermatologist	NR	55-106	None	C / 3
Yap, 1994 (S)[57]	1990	2571	DOC	Dermatologist	Y	NR (all ≥65)	0.3 (8)	B / 3
Young, 1958 (US)[58]	NS	330	DOC and private practice	Dermatologist	NR	60-94	8.2 (27)	C / 3
Zagula-Mally, 1974 (US)[59]	1969-1971	978	Household visits	Nurse, partly revisited by dermatologist	N	NR	Overall: 3.4 (33) ≥75: 10 (7)	B / 4

Abbreviations: BCC, basal cell carcinoma; DOC, dermatology outpatient clinic; Hist, histological; N, no; NA, not applicable; NH, nursing home; NR, not reported; PHI, permanent healthcare institution; QRS, quality rating scheme; S, Singapore; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; UK, United Kingdom; US, United States; y, years; Y, yes (all cases histologically confirmed). [a] *Stratification by age group only viewed if provided;* [b] *Depending on clinical and/or histopathological diagnosis made. STROBE and QRS classification as mentioned in Table 1.*

Table 3 Development of multiple basal cell carcinoma in the oldest-old

Source	Period	Population size[a]	Effect of increasing age on BCC to BCC risk[b]	Definition mult. BCC[c]	Age-group, y	Proportion mult. BCC[d], %	STROBE / QRS
Czarnecki, 1991 (Australia)[63]	1989-1990	575	NR	≥3	75-84	48.8	C / 3
					≥85	45.5	
Flohil, 2011 (Netherlands)[64]	2004-2009	2483	Increasement	≥2	≥80	27.6	A / 3
Karagas, 1992 (US)[65]	1980-1986	1735	Increasement	NR	NR[e]	NR	A / 2
Kiiski, 2010 (Netherlands)[66]	1990-2007	524 (10 296 controls)	Decreasement	≥2	≥75	26.3	A / 2
Levi, 2006 (Switzerland)[67]	1976-2003	1868	Decreasement	NR	NR	NR	B / 3
Ramachandran, 2002 (UK)[68]	1991-1998	747	Increasement	NR	NR	NR	B / 2
Robinson, 1987 (US)[69]	NR (5-year period)	1000	No correlation found	NR	NR	NR	B / 2
Van Iersel, 2005 (Netherlands)[70]	1993-1998	237	Increasement	≥2	>75	43	B / 3

Abbreviations: BCC, basal cell carcinoma; mult, multiple; NR, not reported; QRS, quality rating scheme; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; UK, United Kingdom; US, United States; y, years.[a] Numbers of patients with at least one basal cell carcinoma; [b] Risk to develop a subsequent basal cell carcinoma after an initial basal cell carcinoma; [c] Numbers of tumors; [d] In case only numbers were described proportions were calculated; [e] Patients aged 85 years or older at baseline were excluded. STROBE and QRS classification as mentioned in Table 1.

Clinicopathological features

Subtypes of basal cell carcinoma

Two studies found provide exact data considering the different subtypes of BCC among the oldest-old (Table 4).[71,72] In both studies nodular BCC (nBCC) was the most common subtype of BCC (51.7%-60.7%). In the oldest study[71] no significant correlations were found between subtypes of BCC and the age categories described. The other study[72] showed that superficial BCC (sBCC) were relatively more common among younger patients compared with older adult patients (43% vs 27%; OR, 2.0; 95%CI, 1.1-3.8), whereas no significant influence of age was found for the other subtypes. No data regarding changes of subtype-distribution among the oldest-old over time were found.

Body site distribution

It was shown in different studies that the proportion of BCC in the head and neck region increases with increasing age, while the proportion of truncal BCC seems to decrease.[12,72] Three studies were found presenting specific data on body site distribution in the oldest-old (Table 5).[72-74] Since different categories of body sites are used within the studies, comparison is limited to the categories universally mentioned. A notable higher proportion of truncal BCC is described by Betti et al.[72] compared to the 2 older studies, which could be an indication for a shift over time with a relative increase of truncal BCC.

Tumor size and depth

There is conflicting literature regarding the relation between increasing age and both tumor size and depth. In 1 study, larger BCC were independently associated with increasing age,[75] while another study showed no significant association.[76] It was shown in several studies that the mean age of patients with giant BCC (≥5 cm or ≥10 cm in greatest diameter, definition dependent on study) was comparable with patients with smaller BCC.[77-79] Furthermore, Welsch et al.[80] showed a significant correlation of increasing age with increasing tumor depth in patients with BCC, while Takenouchi et al.[81] could not find this correlation.

Table 4 Subtypes of basal cell carcinoma in the oldest-old

Source	Period	Population size[a]	Hist. confirmation	Age-group, y	Subtype classification	Proportion per subtype[b], %	STROBE / QRS
Betti, 1995 (Italy)[71]	NR (5-year period)	693 (693)	Y	81-90	nBCC	60.7	B / 3
					sBCC	12.5	
					i/morfBCC	25.0	
					Pinkus	1.8	
				>90	nBCC	72.7	
					sBCC	9.1	
					i/morfBCC	18.2	
					Pinkus	0.0	
				Both (≥81)	nBCC	62.7	
					sBCC	11.9	
					i/morfBCC	23.9	
					Pinkus	1.5	
Betti, 2009 (Italy)[72]	1994-2006	173 (175)	Y	≥90	nBCC	51.7	B / 3
					sBCC	27.0	
					i/morfBCC	21.3	

Abbreviations: hist, histological; i/morfBCC, infiltrative/morpheaform basal cell carcinoma; nBCC, nodular basal cell carcinoma; NR, not stated; Pinkus, fibroepithelioma of Pinkus; QRS, quality rating scheme; sBCC, superficial basal cell carcinoma; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; y, years; Y, yes (all cases histologically confirmed). [a] *Numbers of patients with basal cell carcinoma (number of basal cell carcinoma);* [b] *In case only numbers were described proportions were calculated. STROBE and QRS classification as mentioned in Table 1.*

Table 5 Body site distribution of basal cell carcinoma in the oldest-old

Source	Period	Population size[a]	Hist. confir-mation[b]	Age-group, y	Body site classifica-tion	Proportions per body site[c],			IRs[d]			STROBE / QRS
						M	*F*	*Total*	*M*	*F*	*Total*	
Betti, 2009 (Italy)[72]	1994-2006	173 (175)	Y	≥90	Head/neck:	NR	NR	57.3	NR	NR	NR	B / 3
					Trunk:			31.5				
					Limbs:			11.2				
Fears, 1982 (US)[73]	1971-1972 and 1977-1978	6645 (6645)	N (>95%)	75-84	Head/neck[e]:	91.4	87.6	NR	615.4	307.5	NR	B / 2
						84.8	85.4		588.0	297.4		
						84.3	85.1		436.6	280.4		
						85.6	87.8		541.4	268.3		
					Other[4]:	8.6	12.4	NR	57.9	43.5	NR	
						15.2	14.6		105.0	50.9		
						15.7	14.9		81.5	49.3		
						14.4	12.2		91.3	37.1		
Levi, 1988 (Switzer-land)[74]	1976-1985	3811 (3811)	N (>99%)	75-84	Head/neck:	73.8	82.5	78.2	326.3	219.5	NR	B / 3
					Trunk:	16.3	9.8	13.0	72.2	26.0		
					Upper limbs:	3.2	1.1	2.1	14.2	2.9		
					Lower limbs:	3.2	5.3	4.3	14.2	14.2		
					Other:	3.5	1.3	2.4	15.2	3.5		

Table 5 Body site distribution of basal cell carcinoma in the oldest-old (continued)

Source	Period	Population size[a]	Hist. confirmation[b]	Age-group, y	Body site classification	Proportions per body site[c],			IRs[d]			STROBE / QRS
						M	*F*	*Total*	*M*	*F*	*Total*	
Levi, 1988 (Switzerland)[74] (continued)	1976-1985	3811 (3811)	N (>99%)	≥85	Head/neck:	83.4	83.1	83.4	496.3	299.1	NR	
					Trunk:	9.5	9.4	9.4	56.4	33.7		
					Upper limbs:	4.8	2.5	3.4	28.2	9.0		
					Lower limbs:	1.0	1.9	1.5	5.6	6.7		
					Other:	1.0	3.1	2.3	5.6	11.2		

Abbreviations: F, female; hist, histological; IRs, incidence rates; M, male; N, no; NR, not reported; QRS, quality rating scheme; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; US, United States; y, years; Y, yes (all cases histologically confirmed). [a] *Numbers of patients with basal cell carcinoma (number of basal cell carcinoma);* [b] *proportions of histopathologically confirmed tumors given between parentheses when reported;* [c] *In case only numbers were described proportions were calculated, proportions given in %;* [d] *Crude age-specific IRs per 100 000 person-years;* [e] *Separate proportions and incidence rates are given for the two periods and the two locations included in the study (in descending order: Minneapolis 1971-1972, Minneapolis 1977-1978, San Francisco 1971-1972, San Francisco 1977-1978). STROBE and QRS classification as mentioned in Table 1.*

Metastatic basal cell carcinoma

Metastases from BCC rarely occur, with an incidence of .0028% to .55%.[82-84] In metastatic basal cell carcinoma (mBCC) the mean age of onset of the primary tumor was shown lower compared with the general population of patients with BCC,[82-86] ranging from 47.4 to 57.1 years with a mean interval to the diagnosis of mBCC of 8.0 to 16.9 years.[83,84,86] Von Domarus et al.[82] suggested 2 possible explanations for this discrepancy in age distribution: (1) older adults patients may not live long enough to develop metastases from BCC, and (2) BCC in younger patients may have a more aggressive clinical behavior. Moreover, a review and survival analysis of all mBCC cases published in English literature between 1981 and 2011 did not show a relation between age and either the incidence of mBCC or the survival.[86]

Impact on quality of life

Nonmelanoma skin cancer (including BCC) seem to have little overall impact on (dermatology-specific) health-related quality of life (HRQoL) and conflicting data exist regarding the influence of age on HRQoL in patients with BCC (Table 6).[87-91] No studies focusing specifically on the oldest-old were found.

Table 6 The relationship of age and impact on health-related quality of life in patients with nonmelanoma skin cancer

Source	Setting	Tumor type	Period	Population size	Instrument(s) used	Findings	STROBE / QRS
Rhee, 2004 (US)[87]	MMS clinic	NMSC	2001-2002	121[a]	DLQI	Low impact of NMSC on HRQoL, no overall change in DLQI pre- and post-treatment, no influence of age on outcomes	A / 2
Rhee, 2004 (US)[88]	MMS clinic	NMSC	2001-2002	121[a]	SF-36, FACT-G	Low impact of NMSC on HRQoL, no overall change in DLQI pre- and post-treatment, no influence of age on outcomes	A / 2
Rhee, 2007 (US)[89]	MMS clinic	NMSC	2005-2006	211	Skin cancer index	A greater impact of NMSC on HRQoL and a greater improvement of HRQoL after treatment was noticed in younger patients compared to older patients (<50 years vs. ≥50 years)	A / 2
Chen, 2007 (US)[90]	Private practice and veterans affair clinic	NMSC	1999-2000	633	Skindex-16	Pre- and post-treatment impact of NMSC on HRQoL was not found to be related to age	A / 2
Caddick, 2013 (UK)[91]	Skin cancer clinic	NMSC	2008-2010	53	Skin cancer index	Overall and emotional domain HRQoL scores improved more after surgical treatment with increasing age	A / 2

Abbreviations: DLQI, Dermatology Life Quality Index; FACT-G, Functional Assessment of Cancer Therapy-General; HRQoL, health-related quality of life; MMS, Mohs micrographic surgery; NMSC, nonmelanoma skin cancer; QRS, quality rating scheme; SF-36, 36-Item Short Form Health Survey; STROBE, STrengthening of Reporting of OBservational studies in Epidemiology; UK, United Kingdom; US, United States. [a] *Same study population used in both studies. STROBE and QRS classification as mentioned in Table 1.*

Discussion

This systematic review emphasizes the high and growing incidence of BCC in the oldest-old and often frail population. An overview of both previous research as well as knowledge gaps regarding BCC in the oldest-old is provided. A summary of key findings based on the quality of evidence found in this systematic review is given in Table 7.

In the oldest-old population incidence rates of BCC are higher among men and most BCCs are of the nodular subtype and found in the head and neck region. Inconclusive data exists regarding increasing age and the risk to develop a subsequent BCC. No data regarding impact of BCC on quality of life in patients aged 80 years and over were found and inconclusive data regarding the relationship of age and impact of BCC on quality of life were found.

It was previously shown that the burden of BCC is often underestimated in the literature, for instance because most population-based cancer registries do no register data regarding BCC. Several other reasons that might especially apply to the oldest-old could attribute to this underestimation: (1) data in most studies are derived from pathology databases, although a significant number of BCC (ranging from 0.7-24.1%) is clinically diagnosed without histological confirmation,[92] and (2) most BCC registries solely register the first primary BCC in a patient, although subsequent BCC are common.[62] Cases of BCC in the oldest-old are relatively often of the nodular subtype and located in the H&N region compared with younger patients, while the number of sBCC and truncal localization seems to decrease with older age. With the aging of the current younger populations, it could be expected the subtype and body site distribution in the oldest-old will change along over the course of the next couple of decades.

Medical decision making in the oldest-old might be challenging, especially in a typically nonfatal slowly progressive condition like BCC. Therefore, recommendations for screening and treatment are not easily made. For instance, patients may not live long enough to benefit from treatment, while treatment complications could result in a reduced HRQoL. On the other hand, general prognostication could be difficult and a decision not to treat a BCC could have a substantial adverse outcome if a patient lives longer than expected. Data regarding the expected impact of BCC on HRQoL on both the short and longer term could be of value in these situations, but is currently lacking as shown in this review.

Given the rising incidence of BCC and aging of the world population, dermatologists are expected to be increasingly confronted with dilemmas in medical decision making. Guidance

from epidemiologic and clinicopathological data could be of value to overcome these dilemmas. However, as shown in this systematic review, available data from the current literature is limited. Therefore, future research should focus more specifically on BCC in the oldest-old, together with prognostication and their relation with HRQoL on both the short and longer term.

Limitations

Several limitations in this systematic review should be addressed. Important differences between the study populations (e.g. geographic location, population size, racial and cultural differences) and used methods (e.g. diagnostic criteria, definitions and categorization of outcome variables, handling multiple or recurrent tumors) were noted among the included studies. Therefore, comparison, interpretation, and generalization was limited between the included studies. Furthermore, based on the exclusion criteria in this study, potential studies of interest could have been missed (e.g. language bias owing to exclusion of studies not available in English or Dutch).

Conclusion

The incidence of BCC among the oldest-old is high and increasing. Epidemiologic and clinicopathological data from current literature provide only limited guidance in clinical decision making owing to heterogeneity and scarcity. Future research should focus more specifically on BCC in the oldest-old, together with prognostication and their relation with HRQoL on both the short and longer term.

Table 7 Summary of findings based on the quality of evidence found in this systematic review

Finding based on this systematic review	QoE[a]	Related references
IRs of BCC increase with increasing age until the 8th decade;	A	8-22,24-32,34
After the 8th decade conflicting data exists regarding a further increase of IRs with increasing age	B	
IRs of BCC in the oldest-old (patients aged 80 years and older) have increased over the past decades;	A	21,24,28,30,35,36
IRs of BCC in younger populations increased more compared to the oldest-old	B	
IRs of BCC in the oldest-old are higher among men compared to women in most populations	A	8-12,14,16,17-23,24-29,31-33
Nodular BCC is the most common subtype of BCC among the oldest-old	B	71,72
Most BCC are located within the head and neck region in the oldest-old	B	72-74
IRs of metastatic BCC do not increase with increasing age;	B	86
In metastatic BCC the mean age of onset of the primary tumor is lower compared with the general population of patients with BCC	B	82-85
Although death owing to BCC is very uncommon, mortality rates are higher for oldest-old patients compared with younger patients	B	60-61
Inconclusive data exists regarding increasing age and the risk to develop a subsequent BCC	B	63-70
No data regarding impact of BCC on quality of life in oldest-old patients were found and inconclusive data regarding the relationship of age and impact of BCC on quality of life was found	B	87-91

Abbreviations: BCC, basal cell carcinoma; IRs, incidence rates; QoE, quality of evidence.

[a] Quality of evidence: A, based on systematic review/meta-analysis of good quality cohort studies that can apply to most patients; B, based on systematic review/meta-analysis of lower quality cohort studies with inconsistent results that may vary depending on circumstances or patients or societal values; retrospective cohort studies; case-control study; C, based on consensus guidelines, usual practice, expert opinion, case series (levels of evidence for most individual studies in this review are described in Tables 1-6).

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Supplemental Table S1 Search strategy and strings used in this systematic review

Search strategy	
Databases searched:	PubMed, Excerpta Medica Database (EMBASE), and Cochrane Library
Period of time searched:	Articles published up to July 18th, 2015 were included
Key words used:	"basal cell carcinoma" or "nonmelanoma skin cancer", combined with each of the following: "epidemiology", "incidence", "prevalence", "morbidity", "mortality", "elderly", and "long-term care facility". The combination of "skin" and "long-term care facility" was also added. Furthermore, all related synonyms found in the Medical Subject Headings (MeSH) database were used
Limit(s):	All search terms were limited to title and/or abstract
Additional studies:	References of all included articles were screened to identify supplementary relevant studies
Search strings[a]:	
Basal cell carcinoma combined with epidemiology, including synonyms/related terms:	
((((((((((((((((((((basal cell carcinoma[Title/Abstract]) OR basal cell carcinomas[Title/Abstract]) OR BCC[Title/Abstract]) OR BCCs[Title/Abstract]) OR sBCC[Title/Abstract]) OR sBCCs[Title/Abstract]) OR nBCC[Title/Abstract]) OR nBCCs[Title/Abstract]) OR rodent ulcer[Title/Abstract]) OR rodent ulcers[Title/Abstract]) OR basalcell carcinoma[Title/Abstract]) OR basalcell carcinomas[Title/Abstract]) OR basal cell neoplasm[Title/Abstract]) OR basal cell neoplasms[Title/Abstract]) OR basal cell tumor[Title/Abstract]) OR basal cell tumour[Title/Abstract]) OR basal cell tumors [Title/Abstract]) OR basal cell tumours[Title/Abstract]) OR basalioma[Title/Abstract]) OR basaliomas[Title/Abstract])) AND (((((((((((epidemiology [Title/Abstract]) OR epidemiological[Title/Abstract]) OR prevalence[Title/Abstract]) OR incidence[Title/Abstract]) OR frequency [Title/Abstract]) OR surveillance[Title/Abstract]) OR occurrence[Title/Abstract]) OR morbidity[Title/Abstract]) OR mortality[Title/Abstract]) OR survival[Title/Abstract]) OR death rate[Title/Abstract])	
Basal cell carcinoma combined with elderly, including synonyms:	
((((((((((((((((((((basal cell carcinoma[Title/Abstract]) OR basal cell carcinomas[Title/Abstract]) OR BCC[Title/Abstract]) OR BCCs[Title/Abstract]) OR sBCC[Title/Abstract]) OR sBCCs[Title/Abstract]) OR nBCC[Title/Abstract]) OR nBCCs[Title/Abstract]) OR rodent ulcer[Title/Abstract])	

Supplemental Table S1 Search strategy and strings used in this systematic review (continued)

Search strings[a]:
Basal cell carcinoma combined with elderly, including synonyms (continued):
OR rodent ulcers[Title/Abstract]) OR basalcell carcinoma[Title/Abstract]) OR basalcell carcinomas[Title/Abstract]) OR basal cell neoplasm[Title/Abstract]) OR basal cell neoplasms[Title/Abstract]) OR basal cell tumor[Title/Abstract]) OR basal cell tumour[Title/Abstract]) OR basal cell tumors[Title/Abstract]) OR basal cell tumours[Title/Abstract]) OR basalioma[Title/Abstract]) OR basaliomas[Title/Abstract])) AND ((((((((((((((elderly[Title/Abstract]) OR aged [Title/Abstract]) OR geriatric[Title/Abstract]) OR older population[Title/Abstract]) OR oldest [Title/Abstract]) OR sexagenarian[Title/Abstract]) OR sexagenarians[Title/Abstract]) OR septuagenarian[Title/Abstract]) OR septuagenarians [Title/Abstract]) OR octogenarian[Title/Abstract]) OR octogenarians[Title/Abstract]) OR nonagenarian[Title/Abstract]) OR nonagenarians [Title/Abstract]) OR centenarian[Title/Abstract]) OR centenarian [Title/Abstract])
Basal cell carcinoma combined with long-term care facility, including synonyms:
((((((((((((((((((((basal cell carcinoma[Title/Abstract]) OR basal cell carcinomas[Title/Abstract]) OR BCC[Title/Abstract]) OR BCCs[Title/Abstract]) OR sBCC[Title/Abstract]) OR sBCCs[Title/Abstract]) OR nBCC[Title/Abstract]) OR nBCCs[Title/Abstract]) OR rodent ulcer[Title/Abstract]) OR rodent ulcers[Title/Abstract]) OR basalcell carcinoma[Title/Abstract]) OR basalcell carcinomas[Title/Abstract]) OR basal cell neoplasm[Title/Abstract]) OR basal cell neoplasms[Title/Abstract]) OR basal cell tumor[Title/Abstract]) OR basal cell tumour[Title/Abstract]) OR basal cell tumors[Title/Abstract]) OR basal cell tumours[Title/Abstract]) OR basalioma[Title/Abstract]) OR basaliomas[Title/Abstract])) AND ((((((((((((((((((((((((halfway house[Title/ Abstract]) OR halfway houses[Title/Abstract]) OR long-term care facility[Title/Abstract]) OR long-term care facilities[Title/Abstract]) OR longterm care facility[Title/Abstract]) OR longterm care facilities[Title/Abstract]) OR assisted living facility [Title/Abstract]) OR assisted living facilities [Title/Abstract]) OR residential care facility[Title/Abstract]) OR residential care facilities [Title/ Abstract]) OR nursing home[Title/Abstract]) OR nursing homes[Title/Abstract]) OR old age home[Title/Abstract]) OR old age homes [Title/ Abstract]) OR home for the aged[Title/Abstract]) OR homes for the aged[Title/Abstract]) OR retirement life care centre(s)[Title/Abstract]) OR retirement life care center(s)[Title/Abstract]) OR continuing care retirement center(s)[Title/Abstract]) OR continuing care retirement centre(s) [Title/Abstract]) OR housing for the elderly[Title/Abstract]) OR permanent health care institution[Title/Abstract])

Supplemental Table S1 Search strategy and strings used in this systematic review (continued)

Search strings[a]:
Nonmelanoma skin cancer combined with epidemiology, including synonyms/related terms:
((((nonmelanoma[Title/Abstract]) OR non melanoma[Title/Abstract]) OR NMSC[Title/Abstract])) AND ((((((((((epidemiology[Title/Abstract]) OR epidemiological[Title/Abstract]) OR prevalence[Title/Abstract]) OR incidence[Title/Abstract]) OR frequency[Title/Abstract]) OR surveillance [Title/Abstract]) OR occurrence[Title/Abstract]) OR morbidity[Title/Abstract]) OR mortality[Title/Abstract]) OR survival[Title/Abstract]) OR death rate[Title/Abstract])
Nonmelanoma skin cancer combined with elderly, including synonyms:
((((nonmelanoma[Title/Abstract]) OR non melanoma[Title/Abstract]) OR NMSC[Title/Abstract])) AND ((((((((((((((elderly[Title/Abstract]) OR aged[Title/Abstract]) OR geriatric[Title/Abstract]) OR older population[Title/Abstract]) OR oldest[Title/Abstract]) OR sexagenarian [Title/Abstract]) OR sexagenarians[Title/Abstract]) OR septuagenarian[Title/Abstract]) OR septuagenarians[Title/Abstract]) OR octogenarian [Title/Abstract]) OR octogenarians[Title/Abstract]) OR nonagenarian[Title/Abstract]) OR nonagenarians[Title/Abstract]) OR centenarian [Title/Abstract]) OR centenarian[Title/Abstract])
Nonmelanoma skin cancer combined with long-term care facility, including synonyms:
((((nonmelanoma[Title/Abstract]) OR non melanoma[Title/Abstract]) OR NMSC[Title/Abstract])) AND ((((((((((((((((((((((((halfway house [Title/Abstract]) OR halfway houses[Title/Abstract]) OR long-term care facility[Title/Abstract]) OR long-term care facilities[Title/Abstract]) OR longterm care facility[Title/Abstract]) OR longterm care facilities[Title/Abstract]) OR assisted living facility[Title/Abstract]) OR assisted living facilities[Title/Abstract]) OR residential care facility[Title/Abstract]) OR residential care facilities[Title/Abstract]) OR nursing home[Title/Abstract]) OR nursing homes[Title/Abstract]) OR old age home[Title/Abstract]) OR old age homes[Title/Abstract]) OR home for the aged[Title/Abstract]) OR homes for the aged[Title/Abstract]) OR retirement life care centre[Title/Abstract]) OR retirement life care centres[Title/Abstract]) OR retirement life care center[Title/Abstract]) OR retirement life care centers[Title/Abstract]) OR continuing care retirement center[Title/Abstract]) OR continuing care retirement centers[Title/Abstract]) OR continuing care retirement centre[Title/Abstract]) OR continuing care retirement centres[Title/Abstract]) OR housing for the elderly[Title/Abstract]) OR permanent health care institution[Title/Abstract]) OR permanent health care institutions[Title/Abstract])

Supplemental Table S1 Search strategy and strings used in this systematic review (continued)

Search strings[a]:
Skin combined with long-term care facility, including synonyms:
(((((((skin[Title/Abstract]) OR cutaneous[Title/Abstract]) OR dermis[Title/Abstract]) OR epidermis[Title/Abstract]) OR dermal[Title/Abstract]) OR epidermal[Title/Abstract])) AND ((((((((((((((((((((((((halfway house[Title/Abstract]) OR halfway houses[Title/Abstract]) OR long-term care facility [Title/Abstract]) OR long-term care facilities[Title/Abstract]) OR longterm care facility[Title/Abstract]) OR longterm care facilities[Title/Abstract]) OR assisted living facility[Title/Abstract]) OR assisted living facilities[Title/Abstract]) OR residential care facility[Title/Abstract]) OR residential care facilities[Title/Abstract]) OR nursing home[Title/Abstract]) OR nursing homes[Title/Abstract]) OR old age home[Title/Abstract]) OR old age homes[Title/Abstract]) OR home for the aged[Title/Abstract]) OR homes for the aged[Title/Abstract]) OR retirement life care centre [Title/Abstract]) OR retirement life care centres[Title/Abstract]) OR retirement life care center[Title/Abstract]) OR retirement life care centers [Title/Abstract]) OR continuing care retirement center[Title/Abstract]) OR continuing care retirement centers[Title/Abstract]) OR continuing care retirement centre[Title/Abstract]) OR continuing care retirement centres[Title/Abstract]) OR housing for the elderly[Title/Abstract]) OR permanent health care institution[Title/Abstract]) OR permanent health care institutions[Title/Abstract])

[a] *The search strings used in PubMed are shown; comparable search strings were used for the other databases (only slightly adapted when necessary to fit in the model of the concerning database; complete search strings are available on request).*

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Improving the applicability of guidelines on nonmelanoma skin cancer in frail older adults: a multidisciplinary expert consensus and systematic review of current guidelines

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Abstract

Background

Balancing treatment decisions in frail older adults with nonmelanoma skin cancer (NMSC) can be challenging. Clinical practice guidelines (CPGs) could provide assistance.

Objectives

To collect and prioritize items related to frail older adults with NMSC for integration into CPGs and to assess the current extent of this integration.

Methods

Items were collected and prioritized by a multidisciplinary working group (29 members) using a modified Delphi procedure and a 5-point Likert scale. To assess current integration of these items in CPGs, a systematic review was subsequently performed by 2 independent reviewers using 5 medical databases (Pubmed, Excerpta Medica Database (EMBASE), the Cochrane Library, SUMsearch, and the Trip Database), websites of guideline developers/databases, and (inter)national dermatological societies.

Results

Prioritization of a final 13-item list showed "limited life expectancy" (mean (SD), 4.5 (0.9)) and "treatment goals other than curation" (4.4 (0.7)) were most desired to be integrated in CPGs; both included in 6 (46%) of the CPGs found (n=13). Attention to "tumor characteristics" and "comorbidities" were included in CPGs most often (100% and 77%, respectively).

Conclusion

More attention to items related to frail older adults in NMSC CPGs is broadly desired, but CPG integration of these items is currently limited. More integration might stimulate more holistic, personalized and patient-centered care in frail older adults.

Introduction

Frailty is described mostly as the vulnerability of an individual to poor homeostatic resolution after a stressor event, which is considered the result of a cumulative decline in the functioning of various physiological systems with increasing age.[1] Medical decision making will be challenging within the growing population of frail older adults worldwide, especially as factors such as limited life expectancy, comorbidities, and logistical limitations (e.g. travel distance, availability of support by relatives) have to be taken into account.[2] Furthermore, guidance from clinical evidence is limited, as frail older adults are often excluded or under-represented in clinical trials.[3-5]

A common dermatological condition among frail older adults in which these challenges are frequently faced is nonmelanoma skin cancer (NMSC).[6-8] On the one hand, most NMSCs generally have a relatively low malignant potential compared to many other types of cancer. This might favor conservative management, especially in case of a limited life expectancy. On the other hand, NMSC can cause considerable morbidity (e.g. pain, secondary infection, or functional impairment) and, in the longer term, even mortality.[9-11] Therefore, weighing potential benefits and risks of treatment together with preferences from patients and/or their families is essential, but not always easily performed.

Clinical practice guidelines (CPGs) are defined as a set of general recommendations intended to optimize patient care, which assist healthcare providers in daily clinical practice.[12] Obviously, it is not possible to include specific guideline recommendations for every possible situation in every individual patient. Therefore, it could be desirable and in the best interest of a patient to depart from a CPG in some circumstances. However, balancing the extensiveness of the content and the specificity of recommendations in a CPG with generally accepted or self-evident aspects of daily clinical practice might be a challenge.

Various studies have shown the potential benefits of integration of certain topics, including healthcare structures, physician's behavior, and patient outcomes in CPGs.[13] Nevertheless, implementation and adherence to CPGs are often suboptimal and influenced by many factors like appropriate inclusion of the needs and preferences of all relevant professional groups, feasibility, and the flexibility to individualize recommendations.[14-15] Previous studies have shown that guidance from CPGs in frail older adults is limited. Firstly, CPGs (together with most healthcare systems) often focus on curative care and pay little or no attention to other treatment goals, like palliation or preservation of function. Furthermore, CPGs often fail to address issues related to frail older adults and, therefore, provide little guidance in the care for this group of patients.[16-20]

In the present study, we aimed to collect items that are considered important in medical decision making in frail older adults with NMSC, and to prioritize them based on whether they should be integrated into NMSC CPGs. Additionally, we assessed how these items are included in the current NMSC CPGs worldwide and provide recommendations for the future.

Materials and methods

Multidisciplinary working group formation

A multidisciplinary working group of Dutch experts was formed. Age, sex, years of experience, and healthcare setting were taken into account to ensure a well-balanced working group.[21] An overview of the working group formation process and represented parties is given in Supplemental Table S1.

Item List Composition and prioritization

A conceptual list of 10 items influencing medical decision making in frail older adults with NMSC composed by the authors. This list was discussed and adapted by a condensed version of the multidisciplinary working group (including at least 1 expert per medical specialty), using a modified Delphi procedure to reach consensus.[22] Consensus was defined as agreement to include an item by all condensed working group members. During the consensus procedure, 5 items were added to the list and 2 items were removed. Furthermore, 2 items were rephrased to enhance distinctness. Consensus was reached after two rounds, and 13 items were included on the final item list. In addition, to prioritize items for integration into CPGs, participants in the extended working group were asked to provide the items with a score using a 5-point Likert scale. A higher score indicates the item is more desired to be included in CPGs.

Systematic review of literature

A comprehensive review of literature was performed independently by 2 authors (SL and LvV) to identify CPGs concerning NMSC. An initial search was performed using PubMed, Excerpta Medica Database (EMBASE), and the Cochrane Library. In addition, websites of guideline developers/databases and (inter)national dermatological societies, as well as SUMsearch and the Trip Database, were searched for relevant guidelines not yet identified.
An overview of the search strategy, selection criteria, and data sources used is presented in Supplemental Tables S2 and S3. This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[23]

Guideline assessment

Included CPGs were assessed for inclusion of each item from the developed item list (yes or no) and the place in the CPG (in recommendations, only in plain text, or not further specified). Furthermore, the overall quality and reporting of the CPGs were assessed using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, an internationally recognized and validated instrument to evaluate the quality of guidelines.[24] The AGREE II instrument consists of 23 items distributed over 6 domains. Every item is scored by a 7-point Likert-scale (from 1 = strongly disagree to 7 = strongly agree), after which domain scores could be calculated and presented as proportions, following the user manual (http://www.agreetrust.org). Guideline assessment was performed by 2 independent reviewers (SL and RB), both experienced in guideline appraisal. All available appendices and supplementary documents were included in the assessment.

Statistics

Statistics were reported following the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines.[25] Categorical variables were expressed as numbers and percentages. Continuous variables were expressed as means and standard deviations (SD) or medians and ranges, dependent on the distribution of data. Representativeness of the working group members was tested by separately comparing the distribution in age, sex and healthcare setting for the members working in primary care (general practitioners and elderly care physicians) and secondary (or tertiary care) with the corresponding overall populations of physicians in the Netherlands.[26-27] Data collection and analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (IBM Corporation, Armonk, New York, United States).

Results

Multidisciplinary working group characteristics

The condensed and extended working group, the former for composition and the latter for prioritization of the item list, consisted of 11 and 29 members, respectively. The working group characteristics are given in Table 1. A relatively large number of medical specialists in the working group works in academic hospitals as compared to the overall population of medical specialists (57% vs. 20%, respectively).

Prioritization of the final list

The final list of prioritized items to be integrated in CPGs is shown in Table 2. The mean overall items score (SD) was 3.9 (0.9). Highest scores were given to the items "limited life

expectancy" and "treatment goals other than curation": 4.5 (0.9) and 4.4 (0.7), respectively. The lowest scores were given to the items "performance of skin self-examination" and "legal status / impaired capacity to give informed consent": 3.3 (0.7) and 3.3 (0.9), respectively. No scores were missing.

Table 1 Multidisciplinary working group characteristics (n=29)

Characteristics	Values
Age, mean (SD), y	50.1 (7.4)
Male sex, n (%)	18 (62)
Discipline, n (%):	
Dermatologist	13 (45)
Plastic surgeon, otorhinolaryngologist, oral and maxillofacial surgeon, radiation therapist, and geriatrician	2 (7) each
Elderly care physician	3 (10)
General practitioner	3 (10)
Experience[a], mean (SD), y	17.3 (7.0)
Healthcare setting, n (%)[b]:	
General hospital	11 (38)
Academic hospital	13 (45)
Other	9 (31)

Abbreviations: SD, standard deviation; y, years. [a] Residency years excluded; [b] Some working group members work in multiple healthcare settings. No missing data.

Guideline search and selection

The initial search for NMSC CPGs resulted in 6878 results, of which 3682 remained after removal of duplicates. After the additional search and screening by title and abstract, 37 full-text articles were assessed for eligibility, and eventually 13 articles were included (28-40). Figure 1 shows the guideline selection process.

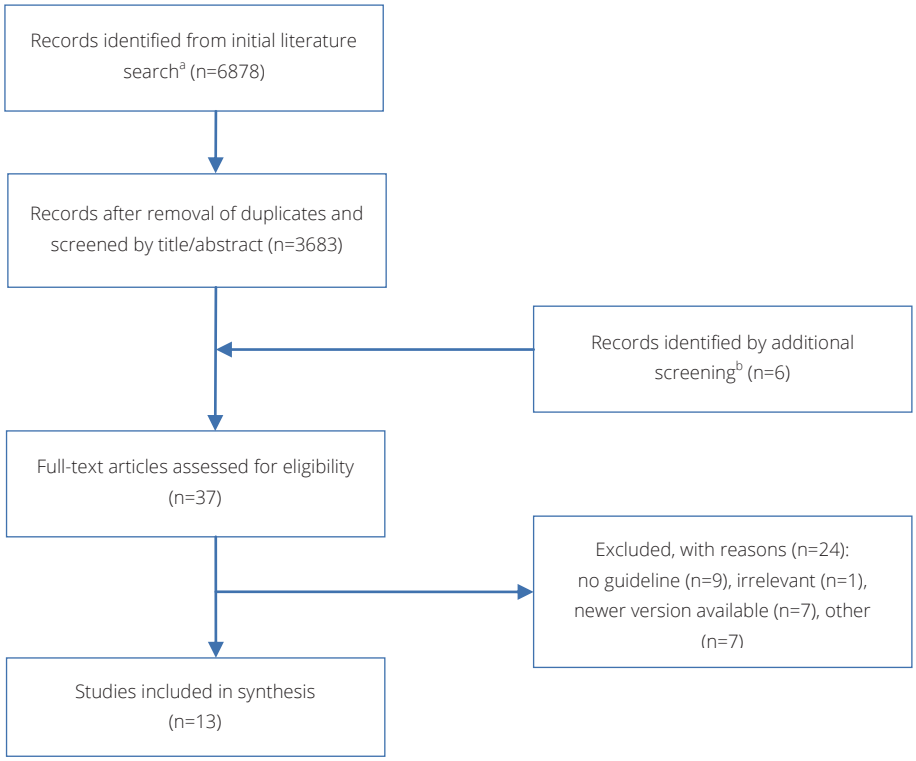
Guideline assessment

Most guidelines are from Europe (n=11) and less than 5 years old (n=7). Squamous cell carcinoma CPGs were most often found (n=6), followed by basal cell carcinoma CPGs (n=5), and CPGs combining both (n=2). The median AGREE II overall score was 50% (range, 36% to

86%) and the median number of items included per guideline was 3 (23%; range, 1 to 9). The guideline characteristics, together with the AGREE II scores and the number of items included per guideline are summarized in Table 3.

All of the individual items from the prioritized list were included in at least 1 guideline. Two items were included in the majority of the CPGs: tumor characteristics (n=13, 100%) and comorbidities (n=10, 77%). The 2 items with the highest prioritization scores ("limited life expectancy" and "treatment goals other than curation") were each included in 6 (46%) CPGs. All other items were included less frequently. Most items were mentioned only in plain text (n=20, 49%), followed by recommendations (n=15, 31%), and "not further specified" (n=10, 20%). A full overview of the individual items and their CPG inclusion is shown in Table 2.

Figure 1 An overview of the guideline selection process in this systematic review on nonmelanoma skin cancer guidelines



[a] Pubmed, Excerpta Medica Database (EMBASE), and the Cochrane library; [b] Websites of guideline developers/ databases, (inter)national dermatological societies, SUMsearch, and the Trip Database.

Table 2 Items desired to be integrated into nonmelanoma skin cancer clinical practice guidelines related to medical decision making in frail older adults, prioritized by the multidisciplinary working group (n=13)

Item	Prioritization score, mean (SD)	Included in CPG, n (%)	Place in CPG, n (%)		
			Recomm.[a]	*Plain text*[a]	*NFS*[a]
Limited life expectancy	4.5 (0.9)	6 (46)	0	4 (67)	2 (33)
Treatment goals other than curation	4.4 (0.7)	6 (46)	1 (17)	4 (67)	1 (17)
Comorbidities	4.2 (0.7)	10 (77)	0	8 (80)	2 (20)
Tumor characteristics	4.1 (0.8)	13 (100)	10 (77)	0	3 (23)
Cognitive impairment	4.0 (0.7)	2 (15)	0	2 (100)	0
Limited possibilities to visit hospital/clinic	4.0 (0.9)	4 (31)	2 (50)	1 (25)	1 (25)
Option of follow-up by primary care physician	4.0 (0.9)	1 (8)	0	1 (100)	0
Family involvement in medical decision making	3.9 (1.0)	1 (8)	0	1 (100)	0
Functional impairment	3.9 (0.6)	1 (8)	0	1 (100)	0
Treatment compliance	3.8 (0.9)	2 (16)	1 (50)	1 (50)	0
Primary care physicians involvement in medical decision making	3.7 (1.0)	1 (8)	1 (100)	0	0
Legal status / impaired capacity to give informed consent	3.3 (0.9)	1 (8)	0	1 (100)	0
Performance of skin self-examination	3.3 (0.7)	1 (8)	0	0	1 (100)

Abbreviations: CPG, clinical practice guideline; NFS, not further specified; Recomm, recommendations; SD, standard deviation. Higher scores indicate the item is more desired to be included in clinical practice guidelines; Values may not add up due to rounding. [a] *items included in CPG-recommendations, only in plain text or not further specified.*

Table 3 An overview of included guidelines and the results of the guideline assessment (n=13)

First author, year[a]	Country or region	Initiating organization(s)	CPG topic[b]	AGREE II Domain scores, %[c]						AGREE II Overall score, %	Items included in CPG, n (%)[d]
				1	*2*	*3*	*4*	*5*	*6*		
Marks, 2008[28]	Australia	CCA, ACN	Both	69	79	38	90	59	61	64	6 (46)
Stratigos, 2015[29]	Europe	EDF, EADO, EORTC	SCC	64	38	49	60	18	68	50	4 (31)
Trakatelli, 2012[30]	Europe	EDF	BCC	48	31	31	71	27	68	43	2 (15)
Bonerandi,2009[31]	France	SFD	SCC	88	81	77	93	45	82	86	9 (69)
Dandurand, 2004[32]	France	SFD, ANAES	BCC	76	57	41	74	39	14	50	3 (23)
Breuningen, 2012[33]	Germany	DKG, DDG	SCC	31	36	26	71	21	61	36	2 (15)
Hauschild, 2012[34]	Germany	DKG , DDG	BCC	31	36	24	71	21	61	36	4 (31)
Kelleners, 2014[35]	NL	NVDV	BCC	88	76	88	90	54	64	86	5 (38)
Krekels, 2010[36]	NL	NVDV	SCC	90	83	80	88	38	39	79	2 (15)
Proby, 2014[37]	Scotland	SIGN	SCC	98	83	79	88	95	75	86	3 (23)
Motley, 2009[38]	UK	BAD	SCC	71	33	30	60	41	14	43	3 (23)
Telfer, 2008[39]	UK	BAD	BCC	60	36	34	71	43	43	50	4 (31)
Miller, 2012[40]	US	NCCN	Both	57	45	25	69	38	50	43	1 (8)
			Median	67	55	48	77	41	54	50	3
			Range	31-98	31-83	24-88	60-93	18-95	14-82	36-86	1-9

Abbreviations: ACN, Australian Cancer Network; AGREE II, Appraisal of Guidelines for Research and Evaluation II instrument; ANAES, French National Agency for Accreditation and Evaluation in Healthcare; BAD, British Association of Dermatologists; BCC, basal cell carcinoma; CCA, Cancer Council Australia; CPG, clinical practice guideline; DDG, German Society

of Dermatology; DKG, German Cancer Society; EADO, European Association of Dermato-Oncology; EDF, European Dermatology Forum; EORTC, European Organization for Research and Treatment of Cancer;NCCN, National Comprehensive Cancer Network; NL, the Netherlands; NVDV, Dutch Dermatological and Venereological Society; SFD, French Dermatology Society; SIGN, Scottish Intercollegiate Guidelines Network; SCC, squamous cell carcinoma; UK, United Kingdom; US, United States.

[a] Year of authorization; [b] BCC, SCC, or both; [c] AGREE II Domains include (1) scope and purpose, (2) stakeholder involvement, (3) rigour of development, (4) clarity of presentation, (5) applicability, and (6) editorial independence; [d] Items related to frail older adults in relation to nonmelanoma skin cancer care.

Discussion

In this study we collected items considered important in medical decision making in frail older adults with NMSC and prioritized them based on whether they should be integrated into NMSC CPGs. It was shown that many items were desired to be integrated in NMSC CPG, but currently the overall CPG integration is limited.

The importance of frailty among older adult patients with cancer and integration of appropriate considerations into CPGs is increasingly acknowledged. Multiple organizations and taskforces have published position papers and guidelines on this topic.[41-43] However, in agreement with this study, previous studies in various fields of medicine showed that attention to frailty-related items like comorbidity and treatment goals other than curation in CPGs is still limited.[16-20,44-45]

The items from this study show a high level of agreement with existing literature on important domains in geriatric oncology.[43,46-47] The expert panel in geriatric oncology in the study from O'Donovan et al. rated functional status, followed by comorbidities and cognition as the most important domains influencing treatment decisions, which were also included in this study although differently prioritized.[47] On the other hand, other domains like mood and nutritional status were not included in this study. Although most of these domains were initially discussed in the working group, they were not included eventually because they were considered of limited additional relevance in the context of treatment of NMSC.

Of course, the items within this study do not apply solely to the population of frail older adults and should be integrated in medical decision making in every patient. However, we specifically focused on frail older adults because in our experience medical decision making is more frequently influenced by the mentioned items in this population, compared to the younger, less frail and often less dependent population.

Based on the outcomes of this study we suggest to include at least the following items in a CPG on NMSC: (1) limited life expectancy, (2) treatment goals other than curation, (3) comorbidities, and (4) tumor characteristics. These items could be integrated in CPG in several ways, e.g. in a dedicated section on general considerations or implementation of the CPG in daily practice or in the discussion of each individual recommendation. The items should be clearly described and easily identifiable.

The other items could certainly be of added value, but we think these should be weighed in relation to the objectives and health questions covered by the guideline (e.g. specific focus

on prevention, one treatment option), the target population, the target users of the CPG (e.g. dermatologists, general practitioners, multiple disciplines), and the characteristics of the healthcare system(s) in which the guideline will be applied (e.g. the existence and role of general practitioners).

Furthermore, we think that participation of a geriatrician and/or elderly care physician, as well as involvement of patients, in the guideline development process will assist in providing proper attention to frail older adults.

Integration of frailty-related items within CPGs might stimulate a more holistic, personalized, and patient-centered care instead of the more tumor-centered care which seems to have become the current standard. Also, integration of more frailty-related items in CPGs might lead physicians to feel more empowered to deviate from regular protocols in the best interest of a patient, especially since CPGs are more and more used as quality indicators and performance incentives by health policy makers.[48]

Nevertheless, we acknowledge that integration of frailty-related items in CPGs does not necessarily mean a change in daily clinical practice and/or patient outcomes. Therefore, attention to other factors which could lead to the mentioned change of perspective in healthcare (e.g. education of healthcare providers, evaluation and adaptation of current healthcare systems, multidisciplinary approaches, usage of screening instruments on frailty etc.) remains important as well.

Also, we would like to emphasize the importance of paying enough attention to patient preferences and shared-decision-making in busy daily dermatological practice. This is closely related to several items collected in this study, like cognitive impairment and an impaired capacity to give informed consent. Cognitive impairment is typically defined as the loss of one or more cognitive functions (e.g. memory or problem solving), which could be seen as a continuum ranging from mild (e.g. mild cognitive impairment) to severe (e.g. end-stage dementia).[49] It might be difficult to estimate a patient's cognitive functioning and the ability to provide informed consent. Therefore, we think in case of doubt the threshold to consult close relatives or other healthcare providers related to the patient should be low.

The recognition of frailty in daily dermatological practice can be challenging, and screening tools to detect frailty and assist in medical decision making might be helpful. An increasing body of literature is available on detecting frailty in oncology by geriatric assessment (GA) and related screening tools.[50] The goals of GA is to determine the medical, psychosocial and functional capabilities of an older adult patient to compose an integrated treatment

plan.[43,51] GA can assist in identifying frailty, help making tailored treatment decisions, and might optimize patient outcomes.[43,49,50]

Several methods are described to perform GA, ranging from multidisciplinary but time-consuming comprehensive geriatric assessment (CGA) to less extensive, derivative screening methods like the Vulnerable Elders Survey-13 (VES-13), Geriatric 8 (G8), or Groningen Frailty Index (GFI).[43,46] However, no studies on NMSC were found and extrapolation of available data from studies on other types of cancer seems limited by factors such as the relatively low malignant natural course of NMSC and the generally less intense and less complex treatment regimes with little adverse events compared to many other types of cancer. Still, the general principles and goals of GA and frailty screening are universal and could be useful in the field of NMSC. Future research should focus on the potential effects and added value of GA and derivative screening tools in frail older adults with NMSC.

The results and recommendations in this study could be of interest to CPG development in general, as most items are not restricted to NMSC.

Limitations

Despite the thorough conceptualization and discussion of the different items within the working group, some overlap and potential misinterpretation could have occurred. The study was performed in the Netherlands including Dutch physicians, which should be kept in mind when generalizing the results. No patients were included in the working group. We acknowledge the importance of including patient preferences and shared decision making, and we would like to suggest future research should focus on this in more detail. The working group formed for this study included a relatively large number of medical specialists working in academic medicine. This could be explained by the large number of medical specialists from academic hospitals directly participating in the activities of medical societies (for instance national guideline committees) and who were therefore delegated to the working group in this study. However, comparison of the working group members with the overall population of physicians showed no important differences considering age and gender for both medical specialists and primary care physicians, indicating an appropriate representativeness regarding these characteristics. Furthermore, it may be that assessed CPGs received low scores on item inclusion despite of the inclusion of frailty-related content, when this content could not be classified into the assessed items on the list. Nonetheless, neither of the reviewers noticed any important (mis)classification bias.

Conclusion

More attention for items related to frail older adults in NMSC CPGs is broadly desired and integration of these items into current CPGs is limited. More integration might stimulate a more holistic, personalized and patient-centered care.

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Supplemental Table S1 An overview of represented parties included in a working group considering nonmelanoma skin cancer care in frail older adults

Working group formation:	
A multidisciplinary working group of experts was formed consisting of representatives from several medical specialities (as shown below). Age, gender, years of experience and healthcare setting were taken into account to ensure a well-balanced working group. All Dutch medical societies related to the mentioned medical specialties were asked to delegate a representative with special affinity regarding nonmelanoma skin cancer and/or frail older adults. Moreover, representatives of the national dermato-oncology working group, the national guideline committees (in both primary and secondary care), and a national network of dermatologists with special interest in geriatric dermatology were also included. Finally, the working group was completed and further balanced with members from several regional healthcare settings.	
Medical specialties included:	**Representation from:**
Dermatology	Dutch Dermatological and Venereological Society[a] and national network of dermatologists with special interest in geriatric dermatology
Plastic surgery	Dutch Society for Plastic Surgery
Otorhinolaryngology	Dutch Society of Otorhinolaryngology and Head & Neck Surgery
Oral and maxillofacial surgery	Dutch Society of Oral and Maxillofacial Surgery
Radiation therapy	Dutch Society of Radiotherapy and Oncology
Geriatric medicine	Dutch Geriatric Society
Elderly care (nursing home) medicine	Dutch Association of Elderly Care Physicians and Social Geriatricians
General practitioner care	Dutch College of General Practitions[b]

[a] Including the national dermato-oncology working group and national guideline committees (basal cell carcinoma and squamous cell carcinoma) and; [b] Including national guideline committee (nonmelanoma skin cancer). The working group was completed and balanced with members from several regional healthcare settings.

Supplemental Table S2 An overview of the databases and websites searched in this systematic review on nonmelanoma skin cancer guidelines

Medical search engines searched:
• Pubmed (http://www.ncbi.nlm.nih.gov/pubmed)
• EMBASE (Excerpta Medica Database) (http://ospguides.ovid.com)
• Cochrane Library (http://www.cochranelibrary.com)
• SUMsearch (http://sumsearch.org)
• Trip Database (https://www.tripdatabase.com)
Guideline developers/databases searched:
• Guidelines International Network (http://www.g-i-n.net)
• National Guidelines Clearinghouse / Agency for Healthcare Research and Quality (http://guideline.gov and http://www.ahrq.gov)
• Ärztliches Zentrum für Qualität in der Medizin (http://www.aezq.de/)
• National Institute for Clinical Excellence (https://www.nice.org.uk/)
• New Zealand Guidelines Group (http://www.health.govt.nz)
• Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk)
• Dutch Association of Comprehensive Cancer Centers (http://www.oncoline.nl)
• Kwaliteitskoepel Medisch Specialisten (http://www.kwaliteitskoepel.nl)
• Dutch College of General Practitioners (http://www.nhg.artsennet.nl)
(Inter)national dermatological societies searched:
• American Academy of Dermatology (https://www.aad.org)
• Australasian College of Dermatologists (https://www.dermcoll.edu.au)
• British Association of Dermatologists (http://www.bad.org.uk)
• Canadian Dermatology Association (http://www.nzdsi.org)
• Deutsche Dermatologische Gesellschaft (http://www.derma.de)
• Dutch Dermatological and Venereological Society (http://www.huidarts.info)
• European Dermatology Forum (http://www.euroderm.org)

Supplemental Table S3 Search strategy and selection criteria used in this systematic review on nonmelanoma skin cancer guidelines

Key word selection and search limitations:
The key words (and synonyms) "basal cell carcinoma, "cutaneous squamous cell carcinoma", or "nonmelanoma skin cancer", combined with "guideline" (both as keyword and separately as limitation) were used. All related synonyms found in the Medical Subject Headings (MeSH) database were also used. All search terms were limited to title and/or abstract. Complete search strategies are shown below:
Search strings:
"Basal cell carcinoma "combined with "guidelines", including synonyms/related terms[a]*:* ((((((((((((((((((((basal cell carcinoma[Title/Abstract]) OR basal cell carcinomas [Title/Abstract]) OR BCC[Title/Abstract]) OR BCCs[Title/Abstract]) OR sBCC[Title/Abstract]) OR sBCCs[Title/Abstract]) OR nBCC[Title/Abstract]) OR nBCCs[Title/Abstract]) OR rodent ulcer[Title/Abstract]) OR rodent ulcers[Title/Abstract]) OR basalcell carcinoma [Title/Abstract]) OR basalcell carcinomas[Title/Abstract]) OR basal cell neoplasm[Title/Abstract]) OR basal cell neoplasms[Title/Abstract]) OR basal cell tumor[Title/Abstract]) OR basal cell tumour[Title/Abstract]) OR basal cell tumors[Title/Abstract]) OR basal cell tumours [Title/Abstract]) OR basalioma[Title/Abstract]) OR basaliomas[Title/Abstract])) AND ((((((((guideline[Title/ Abstract]) OR guidelines[Title/Abstract]) OR recommendation [Title/Abstract]) OR recommendations[Title/Abstract]) OR protocol[Title/Abstract]) OR protocols [Title/Abstract]) OR standard[Title/Abstract]) OR standards[Title/Abstract]); with and with-out "guidelines" as limitation
"Cutaneous squamous cell carcinoma" combined with "guidelines", including synonyms[a]*:* ((((((((skin[Title/Abstract]) OR cutaneous[Title/Abstract]) OR dermis[Title/Abstract]) OR epidermis[Title/Abstract]) OR dermal[Title/Abstract]) OR epidermal[Title/Abstract])) AND ((((((((((((((((((squamous cell carcinoma[Title/Abstract]) OR squamous cell carcinomas [Title/Abstract]) OR SCC[Title/Abstract]) OR SCCs[Title/Abstract]) OR SqCC[Title/Abstract]) OR SqCCs[Title/Abstract]) OR squamouscell carcinoma[Title/Abstract]) OR squamouscell carcinomas[Title/Abstract]) OR squamous cell neoplasm[Title/Abstract]) OR squamous cell neoplasms[Title/Abstract]) OR squamous cell tumor[Title/Abstract]) OR squamous cell tumour[Title/Abstract]) OR squamous cell tumors[Title/Abstract]) OR squamous cell tumours[Title/Abstract]) OR planocellular carcinoma[Title/Abstract]) OR planocellular carcinomas[Title/Abstract]) OR epidermoid carcinoma[Title/Abstract]) OR epidermoid carcinomas[Title/Abstract])) AND ((((((((guideline[Title/Abstract]) OR guidelines[Title/ Abstract]) OR recommendation[Title/Abstract]) OR recommendations[Title/Abstract]) OR protocol[Title/Abstract]) OR protocols[Title/Abstract]) OR standard[Title/Abstract]) OR standards[Title/Abstract]); with and without "guidelines" as limitation

Supplemental Table S3 Search strategy and selection criteria used in this systematic review on nonmelanoma skin cancer guidelines

Search strings:
"Nonmelanoma skin cancer" combined with "guidelines", including synonyms[a]: ((((nonmelanoma[Title/Abstract]) OR non melanoma[Title/Abstract]) OR NMSC[Title/Abstract])) AND (((((((guideline[Title/Abstract]) OR guidelines[Title/Abstract]) OR recommendation[Title/Abstract]) OR recommendations[Title/Abstract]) OR protocol[Title/Abstract]) OR protocols[Title/Abstract]) OR standard[Title/Abstract]) OR standards[Title/Abstract]); with and without "guidelines" as limitation
Article selection criteria:
Title, abstract, full-text screenings were consecutively and independently performed by two authors (SL and LvV). Relevant articles published up to 15-05-2015 were included. When full-text articles were not available online, the Dutch Central Catalogue (PiCarta) and/or the first author was contacted to obtain the article. Exclusion criteria were: full-text not available, non-English/Dutch/German publications, and guidelines written on one therapeutic option (for instance exclusively on photodynamic therapy). Both guidelines regarding only one type of NMSC (basal cell carcinoma or squamous cell carcinoma) as well as guidelines regarding NMSC in general were included. Only the most recent version of each guideline was included. Inconsistencies between the two reviewers were discussed until consensus could be reached. In case no consensus could be reached a third reviewer (MG) was involved.

[a] *Pubmed version; comparable strategies were used in other databases.*

9

General discussion and future perspectives

General discussion and future perspectives

The aims of the studies presented in this thesis were to obtain insights in the current need for, provision of, and quality of general dermatologic care among nursing home patients (Part A of this thesis), and to study current skin cancer care among older adults and provide guidance in medical-decision making (Part B of this thesis). In this chapter the research questions related to these aims, as formulated in **Chapter 1**, will be answered and discussed. In addition, future perspectives will be provided and integrated in this discussion.

Dermatologic care in institutionalized older adults

To obtain insights in the current need for, provision of, and quality of general dermatologic care among nursing home patients, the following research questions were answered in part A of this thesis and will be discussed below:

(1) What is the current need for and provision of dermatologic nursing home care according to nursing home physicians (NHPs) in the Netherlands? (**Chapter 2**)

(2) What is the current role of Dutch dermatologists in dermatologic care provision in nursing homes? (**Chapter 3**)

(3) What are the reasons and barriers for dermatologist consultations in nursing homes? (**Chapter 3**)

(4) How could we improve dermatologic care for nursing home patients? (**Chapters 2 and 4**)

In **Chapters 2 and 3** the current status of dermatologic care among Dutch nursing homes is described from the perspective of Dutch NHPs and dermatologists respectively. In addition, recommendations for improvement of dermatologic care among nursing home patients are described in **Chapters 2 and 4**.

It was found that NHPs are frequently confronted with skin conditions in their patients. The skin conditions NHPs are most frequently confronted with are (pressure) ulcers, eczema, fungal and bacterial infections, pruritus sine material, and skin tumors, which is largely in concordance with previous studies.[1]

Availability of diagnostic and treatment options in nursing homes

Although most conditions are initially diagnosed and treated by NHPs themselves, a lack of availability and experience of NHPs limits the diagnostic and treatment options. This limitation was highlighted by NPHs as one of the most important topics to improve

dermatologic care within nursing homes (**Chapter 2**). Examples of diagnostic and treatment options for which this especially seems to be the case are dermoscopy, punch biopsy, most non-pharmacological treatment options (cryotherapy, curettage, and excision) and some pharmacological treatment options (e.g. topical calcineurine inhibitors, topical imiquimod).

Obviously, availability and experience are highly connected to each other. For example, on the one hand, a physician lacking the experience to take a punch biopsy will be less prone to arrange the logistical possibility to be able to perform this, compared to a more experienced physician. On the other hand, physicians working in a nursing home in which the logistics are available to perform punch biopsies will probably be more prone to do so.

Availability of diagnostic and treatment options is presumably strongly influenced by the balance between the demand and costs. For instance, the costs related to the purchase and maintenance of liquid nitrogen to perform cryotherapy (typically including a barrel and related materials, but also a maintenance contract with a provider) might outweigh the benefits in case of a low demand and/or usage of this treatment option. However, a compromise might be made purchasing a portable dimethyl ether propane-based cryotherapy system (e.g. Histofreezer® or Verruca-freeze®). Although the efficacy of these systems may be inferior to a classic liquid nitrogen system, it provides an opportunity to start gaining experience with cryotherapy.[2-4] Consequently, the demand for cryotherapy may thereby increase and create a situation where the purchase of a classic liquid nitrogen system might become cost-effective after all.

Another example illustrating the balance between demand and costs is the punch biopsy. To create the logistic possibility to perform punch biopsies materials have to be purchased, which is easily organized for a reasonable price. However, setting up an arrangement with a pathology laboratory and the related costs for histopathological analysis might be a greater threshold in daily practice. This is probably largely explained by the funding system of healthcare costs in nursing homes.

Nursing home care is provided under the Long-term Care Act *(Dutch: Wet langdurige zorg)*.[5] This includes an integral budget for all costs related to chronic institutionalized care, including meals, assistance in daily living activities, daycare, nursing, medical care provided by the NHP etc. The latter includes NHP-initiated costs related to diagnosis and treatment of conditions. For example, costs related to a punch biopsy performed by a NHP will be paid from this integral budget and therefore influences the other expenses covered by this integral budget. In contrast, care provided by a dermatologist is provided under the Health Insurance Act *(Dutch: Zorgverzekeringswet)*,[5] which is separately arranged and does not

directly affect the integral budget provided under the Long-term Care Act. Therefore, a punch biopsy performed by a dermatologist is separately financed and will not affect the integral nursing home budget.

The above-mentioned funding system probably leads to a higher threshold for NHPs to perform certain diagnostic and treatment procedures themselves. An example to illustrate this financial friction as once mentioned by a colleague (a NHP): *"Although I have the logistical possibility and skills to perform a punch biopsy, I still refer mr. Jansen to a dermatology outpatient clinic for this, simply because multiple of his nursing home neighbors won't be able to attend their weekly craft hour when I perform the biopsy myself."*

Medical specialist care (including care provided by a dermatologist) should be accessible for everybody after adequate referral. This should be driven by a medical demand and not by a financial one. In times where substitution of care from medical specialists to primary care physicians (including NHPs) is high on the (political) agenda, more attention should be paid to the nursing home settings (this will be discussed in more detail later). Therefore, reconsideration of the current funding system by health policy makers should be given priority.

The experience of nursing home physicians in diagnosing and treating skin conditions

As mentioned, next to the availability of diagnostic and treatment options, experience is considered a key element as well (**Chapter 2**). Experience can be obtained by education in the first place. Several forms of education might contribute to this in varying degrees and on different perspectives. Basic education during medical school or in the form of continuing medical education might create awareness and basic knowledge and skills regarding diagnostic and treatment options in common skin conditions. On the other hand, other more interactive forms of education might contribute to the specific development of technical skills in a higher extent (e.g. interactive workshops, bed-side teaching, accompanying a dermatologist at the outpatient clinic).[6-8]

Although obtaining knowledge and technical skills is important, using them in daily practice on a regular basis is essential to further develop and maintain them. For example, dermoscopy is a very useful diagnostic tool in many skin conditions when adapted by a properly trained physician. However, dermoscopy performed by untrained physicians does not necessarily improve diagnostic accuracy and might even result in misdiagnosis and treatment delay.[9-12]

The ability to perform diagnostic and treatment skills on a regular basis obviously relates to the demand for certain diagnostic and treatment procedures in daily practice. Therefore, it may be helpful to train a restricted number of NHPs with a special interest in dermatology (for instance one or two NHP(s) per nursing home organization, who could be consulted by colleagues when necessary) to maximize the development and maintenance of skills.

Dermatologist consultation

Although diagnosis and treatment of various skin conditions is frequently performed by NHPs, the demand for dermatologist consultation remains high. As shown in **Chapters 2 and 3**, cutaneous (pre)malignancy is by far the most common reason for dermatologist consultation. This was additionally studied in more detail, as described in **Chapter 5** (Part B of this thesis). It was shown that several methods of dermatologist consultation are used, ranging from outpatient clinic consultation, to nursing home consultations by dermatologists, and consultation by phone or using teledermatology. Both NHPs and dermatologists mentioned two forms of dermatologist consultation as important topics to improve dermatologic care in nursing homes, as presented in **Chapters 2 and 4**: (1) to make more and better use of teledermatology, and (2) more live consultation of dermatologists in nursing homes. Both of these consultation forms are discussed in more detail below.

Teledermatology

The usage of teledermatology, a form of digital consultation of a dermatologist through a secured internet connection, is limited in Dutch nursing homes. Only 31.6% of the NHPs have ever used teledermatology, while it is estimated that 60-70% of the Dutch general practitioners currently uses teledermatology.[1,13,14] Telemedicine in nursing homes has several potential benefits, since it may improve nursing home care and it might replace outpatient clinic visits, which often are more difficult to organize. Furthermore, the acceptance of telemedicine by patients, families, and caregivers was generally shown to be high.[15-22]

Previous research has addressed several potential explanations for the discrepancy between the relatively low usage of teledermatology by NHPs on the one hand, while more usage of teledermatology is suggested as a major topic for improvement of nursing home care on the other hand.[1] The followings reasons were mentioned most frequently: unavailability of ICT facilities (23%), unavailability of a camera or not knowing how to make proper photos (23%), unfamiliarity with teledermatology (20%), and financial reasons (17%).

Better education regarding teledermatology for NHPs is expected to help overcome most of the barriers mentioned. Through education, NHPs might become more familiar with the concept of teledermatology, the possibilities, and how to organize this in daily practice. Moreover, potential false assumptions regarding teledermatology could be discussed. For example, it was shown that NHPs often assume that various ICT facilities and/or an expensive, high-tech camera are needed for a teledermatology consultation, while a simple smartphone with teledermatology-app usually will suffice.[1]

Next, as previously mentioned, the funding system seems another important limiting factor for teledermatology usage in daily nursing home practice. NHPs might be more inclined to refer patients to a dermatologist for live consultation instead of using teledermatology, since related costs of diagnostic procedures and treatment after live dermatologist consultation don't have to be paid from the integral budget provided under the Long-term Care Act (but by separate funding though the Health Insurance Act instead).

Furthermore, for general practitioners a special financial construction was started in 2006 to prevent unnecessary referrals to medical specialists and keep as much of the care as possible within the primary care system (the substitution effect). This special financial construction, also called *"Modernisering & Innovatie"* (M&I), arranges (extra) financial compensation for a predefined set of diagnostic or treatment procedures including teledermatology and small surgical procedures, when performed by a general practitioner. Unfortunately, this construction does not apply to NHPs. It is advised to arrange a comparable financial construction for NHPs to optimize care, stimulate the usage of teledermatology, and prevent unnecessary dermatologist referrals.[23]

As described in the introduction of this thesis, it should be mentioned that teledermatology has a lot of advantages, but it also has some important limitations. The most important limitation in the nursing home population probably is the low diagnostic accuracy in case of a solitary (pigmented) lesion, which is the most frequently mentioned reason for a NHP to consult a dermatologist. Another important limitation is the restricted availability of information regarding the context of a patient when using teledermatology, which might limit a holistic care approach. Therefore, availability of other forms of consultation, especially live consultation, remains essential. Teledermatology has a lot to offer in the nursing home population, but will never be able to fully replace live dermatologist consultation.

Live consultation

As described in **Chapter 3**, only one third (30.0%) of the Dutch dermatologists has ever visited a patient within a nursing home for consultation. Meanwhile, over two thirds (68.5%)

of the Dutch dermatologists and dermatology residents are willing to visit patients on location in a nursing home. Furthermore, more live consultation of dermatologists in nursing homes was suggested as one of the most important topics to improve dermatologic care in nursing home patients by both NHPs and dermatologists (**Chapters 2 and 4**). This high demand for a nursing home consultant service by medical specialists seems in accordance with the limited amount of previous research available from Germany and the United States in several fields of medicine.[24-26]

Examples of advantages of live consultation of a dermatologist in a nursing home are:

(1) Nursing home patients do not have to attend the outpatient clinic, which might for instance prevent a lot of stress and discomfort;
(2) Relatives do not necessarily have to take off from work to attend to the dermatologist consultation;
(3) It might be easier for a dermatologist visiting a nursing home to obtain contextual patient information and include this in management recommendations;
(4) It might be easier for a dermatologist to provide more feasible and better implementable management recommendations after a nursing home visit (e.g. because the availability of local wound care products becomes more clear);
(5) It might enhance proper instruction of the nursing home staff and might thereby stimulate treatment compliance;
(6) Live consultation of a dermatologist might have an important educational value for nursing home staff (bed-side teaching).

In **Chapter 3** barriers to perform nursing home visits were described as stated by dermatologists. The most important barriers mentioned were a lack of time and indistinct and/or inadequate financial compensation. Experience from daily practice shows nursing home consultations take a relatively large amount of time compared to consultations in the outpatient clinic and therefore usually generate a relative loss of income when planned instead of regular outpatient clinic consultations. Therefore, a lot of dermatologists plan nursing home visits alongside of their regular outpatient clinic consultations (e.g. during administration time or a day off).

Several tips and tricks may improve efficacy of nursing home consultations, both in terms of time and related costs:

(1) *Clustering patients:* examining multiple patients per single nursing home visit enhances efficiency of a nursing home visit and will reduce relative travel and preparation time. The past couple of years a trend was seen of scaling down (larger) nursing homes by replacing larger locations for smaller, more spread out nursing homes. These trends might interfere with the possibility to cluster patients during a nursing home visit.

(2) *Using predefined dates and time slots:* a smoothly running and effective nursing home visit might be enhanced by clear agreements on dates and time slots of nursing home consultations. This will often prevent unnecessary waiting times for the dermatologist, nursing home staff and patients. Furthermore, this might make it easier for relatives of a patient to attend the consultation if desired.

(3) *Centralization:* using one room in the nursing home for consultations and letting patients come to this room when possible -instead of walking from patient to patient- might further optimize efficiency of a nursing home visit. Obviously, this may not be feasible in some cases (e.g. bedridden patients).

(4) *Optimizing patient referral:* to be able to perform effective nursing home consultations, NHPs should include all essential information needed in their patient referrals, especially when NHPs are not attending the consultations themselves. Examples of information which can be essential are a detailed and explicit reason for referral, information on the patient's general health status, the patient's legal status, functional impairment, expectations, management goals, and (end-of-life) treatment limitations. Furthermore, receiving the patient referrals (including all essential information) prior to the nursing home visit will usually improve a proper preparation.

(5) *Communication:* clear and concise communication between the dermatologist and the nursing home staff on expectations towards each other will enhance a smoothly running and effective nursing home visit and might prevent indistinctness and friction.

(6) *Support:* adequate supporting staff (e.g. a dermatology nurse) might enhance the efficiency of a nursing home visit.

(7) *Preparation:* proper preparation may assist in an effective nursing home visit as well. Preparation might include receiving patient referrals prior to the visit, collecting the necessary material for diagnostic and treatment procedures which might be needed to perform, and/or to discuss all patients with the NHP "on paper" before the actual consultation to further clarify the reason for referral, management goals etc.

(8) *Combination with digital consultation:* as mentioned before combining live consultation in a nursing home with teledermatology might enhance the efficiency of a visit. For example, teledermatology might be used for patient triage to select the patients where a live consultation is needed, or to start pretreatment prior to live consultation to optimize the possibility for examination or treatment (e.g. the removal of crusts or to start preventive antibiotics).

In addition, next to potential advantages and tips and tricks, potential pitfalls of nursing home visits should be addressed as well. Firstly, nursing home consultations by a dermatologist might act as a pull factor. Obviously, lowering the threshold for dermatologist consultation in nursing homes might improve dermatologic care as mentioned before. However, the level of this threshold should be well-balanced and unnecessary referrals (over-referral) should be prevented. Therefore, it is recommendable for both dermatologists and NHPs to pay attention to this balance and to critically evaluate referrals together on a regular basis.

An example to illustrate the pitfall of over-referral, as once mentioned by a colleague (a dermatologist): *"When I had visited nursing home B a couple of times, I noticed that NHPs started to refer patients with skin complaints which they didn't even examined themselves yet. It was almost like when the nursing staff noticed a skin problem in a patient he or she was immediately referred to me."*

Secondly, another potential pitfall of nursing home consultations by a dermatologist on a regular basis is the concept of "getting used to it" (habituation). When NHPs, other nursing home staff, patients and family members become used to the possibility of nursing home consultation, they might start to take this possibility for granted. This doesn't necessarily have to be a problem, but this might jeopardize flexibility and the willingness of a dermatologist to perform nursing home consultations.

An example to illustrate the pitfall of habituation, as once mentioned by a colleague (a dermatologist): *"When I visited nursing home C for the first time a NHP guided me through the building from patient to patient and the patients and nursing home staff were very thankful. But after a couple of times, people got used to my consultations and seem to took it for granted: NHPs stopped guiding me along the patients and nursing home staff told me to come back when their coffee break was over. This is very demotivating, especially when you use your day off to perform these consultations."*

Financial framework

Time and cost investment are the main barriers for dermatologists to perform nursing home visits. A special financial compensation for nursing home visits might stimulate dermatologists to provide nursing home consultations on a more regular basis and to a greater extent. In the ideal situation, overall earnings of an afternoon of nursing home consultations should be comparable with an afternoon of outpatient clinic consultations. Although it will be hardly possible to see the same number of patients in a given part of the day compared with the outpatient clinic in the same time span, the overall earnings for a dermatologist might reach approximate comparability due to elimination of hospital-overhead costs in case of nursing home consultations. The current developments on "anderhalvelijnszorg" (see the introduction of this thesis for more details) may be an opportunity to start a discussion on this subject and to organize a financial arrangement for dermatologists, performing nursing home consultations.

Educational effects

As previously discussed, nursing home consultations by a dermatologist might have an educational value to NHPs and nursing home staff (bed-side teaching principle).[27] However, the educational value might also have an effect the other way around, since dermatologists may also learn about several aspects concerning geriatric medicine during their nursing home visits.

As presented in **Chapters 2 and 3**, we studied to what extent several patient-related factors are taken into account by dermatologists when making medical management decisions in nursing home patients. Scores were provided by both NHPs and dermatologists. Dermatologists provided themselves with higher scores compared to the scores they received from NHPs. Dermatologists also provided themselves with higher scores compared to the scores they provided to dermatologists in general, which might be an indication of self-overestimation. Close co-operation between a dermatologist and NHP might assist leveling out these differences found and help improve care by taking into account each other's points of view and expertise.

Moreover, half of the dermatologists and dermatology residents (50.8%) would like to receive more training in geriatric medicine. This seems to fit the trend shown by many medical specialties and organizations, where the importance of better training in general older adult care medicine is increasingly acknowledged and implemented in medical training programmes and daily clinical practice.[28,29] In 2014 the "CanBetter project", initiated by the Dutch Order of Medical Specialists, resulted in more implementation of older adult care in medical specialty training, including dermatology.[30] This included defining the competences

needed to provide proper healthcare for older adults and implementing these competences and the ways to develop them in national and local dermatologists training programmes. Furthermore, a dedicated session on geriatric dermatology was integrated in the Dutch national educational program for dermatology residents (mandatory for every dermatology resident in the Netherlands). Proper evaluation and further development of the above-mentioned measurements is recommended, to optimize the ultimate impact on healthcare and to make sure predefined goals are achieved.

Final considerations regarding dermatologic care in nursing home patients

In conclusion, a close collaboration between NHPs and dermatologists is the key element to improve dermatologic care in nursing home patients. Multiple forms of consultation, including teledermatology and live consultation of a dermatologist in a nursing home, should be available on a regular basis and could complement each other. Several logistical and financial barriers should be minimized to enable these consultations to a greater extent.

Skin cancer care in frail older adults

In part B of this thesis more specific attention was paid to skin cancer care among older adults. To study current skin cancer care among older adults and provide guidance in medical-decision making, the following research questions were answered and discussed below:

(1) What is the current and potential future role of nursing home physicians (NHPs) in the diagnosis and treatment of (pre)malignant skin lesions among nursing home patients? (**Chapter 5**)

(2) What is the influence of high age and comorbidity in medical decision making and guideline-adherence by dermatologists in older adults with nonmelanoma skin cancer (NMSC) in daily clinical practice? (**Chapter 6**)

(3) What is currently known about the epidemiology and clinicopathological features of basal cell carcinoma (BCC) in the oldest-old to guide healthcare providers and policy makers? (**Chapter 7**)

(4) Which items are considered important in medical decision making in frail older adults with NMSC and should be integrated in NMSC clinical practice guidelines? (**Chapter 8**)

(5) What is the extent of integration of these items in current NMSC clinical practice guidelines worldwide? (**Chapter 8**)

The role of nursing home physicians and dermatologists in skin cancer care

In addition to part A of this thesis the role of NHPs in skin cancer care among nursing home patients was further studied, as described in **Chapter 5**. Although NHPs are frequently confronted with skin cancer or precursor lesions among their patients, the role of dermatologists in skin cancer care remains essential and the demand for dermatologist consultation is high.

However, due to the high prevalence of skin cancer in this patient group on the one hand and the relative barrier to visit a dermatology outpatient clinic or to arrange a dermatologist consultation within the nursing home on the other hand, dermatologists might not be able to meet this demand.

Therefore, it seems especially important for NHPs to have basic knowledge and skills in skin cancer diagnosis and treatment. As shown in **Chapter 5**, a considerable proportion of NHPs provides some extent of skin cancer care, especially in lower risk (pre)malignant lesions (e.g. actinic keratosis, BCC). Furthermore, a significant proportion of NHPs would be willing to increase their extent of skin cancer care providence after better training. Consequently, the demand for better training was high. Comparable results were found in a study among Dutch general practitioners on skin cancer care.[31] A high demand for more training on skin cancer care was also noted by a German study among various caregivers, including NHPs.[32]

In addition, even if NHPs are not comfortable and/or willing to perform more skin cancer care themselves, it is still of vital importance for NHPs to have some basic knowledge regarding skin cancer, for the following reasons:

(1) To be able to recognize a (pre)malignant skin lesion;
(2) To have some understanding about the prognosis and treatment options;
(3) To be able to properly determine when to consult a dermatologist;
(4) To prevent making false assumptions regarding skin cancer in daily clinical nursing home practice, which unfortunately is very common in my experience (e.g. not knowing the tumor prognosis, not knowing some specific (simple) treatment options, or overestimating the burden for a patient choosing a certain treatment option);
(5) To eventually enhance the possibility of active and well-informed participation of NHPs in the decision-making process in skin cancer care, together with the patients, their families, and the dermatologist.

As previously discussed, training a restricted number of NHPs with a special interest in dermatology, including skin cancer care, might optimize the development and maintenance of diagnostic and treatment skills. As in general dermatologic care, the role of NHPs in skin cancer care has (and should have) certain limitations and accessible possibilities to consult a dermatologists to provide skin cancer care still remains of major importance.

Medical-decision making in patients with nonmelanoma skin cancer: the influence of high age and comorbidity and the concept of general prognostication

In the next chapters more attention was paid to medical-decision making in frail older adults with NMSC. Management decisions in frail older adults with NMSC are made on a regular basis in daily dermatologic clinical practice and making a well-balanced management decision in an individual patient might be challenging due to several factors like a limited life expectancy or cognitive impairment.

Clinical practice guidelines (CPGs) are intended to provide a general framework for clinicians based on the best evidence available. Obviously, recommendations in CPGs are not universally applicable. Therefore, guideline deviation should sometimes be considered and may be in the best interest of the individual patient. In **Chapter 6** it was hypothesized that this might especially be the case in patients with a limited life expectancy. Therefore, the influence of two key factors related to limited life expectancy (high age and comorbidity) on medical decision making in NMSC were studied in more detail. It was found that medical decision making and guideline-adherence was not (in squamous cell carcinoma) or only minimally (in BCC) influenced by high age and comorbidity, which contradicted our expectations.

These findings do not necessarily tell us something about the actual quality of care, but can be used as a starting point for a discussion on skin cancer care in frail older adults. Several potential explanations might play a role in these findings. High age and comorbidity may be included in management considerations by treating physicians, but simply are not considered of important influence in optimal skin cancer management and therefore have no or only minor influence. Furthermore, it might also be that high age and comorbidity show only minor influence because the awareness for inclusion of these factors in management considerations is low, or dermatologists might not know how to implement these factors in their management considerations.

Future research should focus in more detail on management decisions in frail older adults with skin cancer. Reliable general prognostication of life expectancy is a key element in further tailoring skin cancer care in this population. Obviously, adequate prediction of the

natural course of a NMSC and the impact on quality of life caused by the tumor and/or treatment should be included as well, and are discussed in more detail later. Previous research on general prognostication showed that estimating the (remaining) life expectancy of a patient is difficult. Although life expectancy closely relates to age, a patient's life expectancy is influenced by several factors, of which comorbidity is considered the strongest and best studied predictor.[33-37] Consequently, clinical decision making merely based on chronological age is considered rather arbitrary, and should therefore be avoided. Although comorbidity-based prognostic indices for older adults certainly have limitations (e.g. in generalizability) and should be used with caution, they might be of assistance in daily practice. Future research on further validation and selection of existing indices in older adults with NMSC and on the feasibility of these indices in daily clinical practice are recommended.

Guidance in medical-decision making by current literature

BCC is the type of skin cancer in which medical-decision making in frail older adults seems to offer the greatest challenges in daily practice. In **Chapter 7** literature was systematically reviewed for data on BCC in older adults (≥80 years) in order to guide clinicians in management considerations and to detect gaps in current knowledge. BCC is a very common tumor in persons aged ≥80 years and the incidence rates are rising. Despite of this commonness, relatively less is known regarding BCC in this patient population. Due to the relatively low-malignant natural course of BCC compared to many other types of cancer, management can be challenging in older adults. Balancing the risk for under- and overtreatment, combined with patients and family preferences, is not always easily performed. It was shown that current literature lacks essential information on many important aspects, like impact on quality of life (in both the short and long term) and prognostication. Therefore, clinicians are only very limitedly guided by current literature in making these management decisions.

Natural course and impact on health-related quality of life

Few studies have examined the natural evolution of BCC in more detail. Only a couple of studies (mostly retrospective) have tried to obtain some exact information regarding growth speed and development of BCC, which mainly include high-risk BCC located within the head and neck area. Based on these available studies it is estimated a high-risk BCC would take 2,4-3,8 years to reach a size of 10 mm in maximal diameter. It is expected these growth rates may be less for low-risk BCC, although faster growth is possible and no reliable predictors for BCC development are currently known.[38] Future studies on the natural course of BCC would be very valuable to help overcome treatment dilemma's in frail older adults.

As stated, also less is known regarding the impact of BCC on health-related quality of life (HRQoL) in general populations with BCC and no specific studies were identified on HRQoL impact of BCC in oldest-old. However, HRQoL is one of the most important keystones on which management decisions should be based, and more studies on this topic are therefore essential. Studies on the impact of HRQoL in BCC can be especially valuable for daily clinical practice when they would be able to detect more information of HRQoL along the natural course of BCC. This is especially important for the longer term impact of BCC on HRQoL, since the currently available studies only focus on the short term HRQoL impact.

In addition, studies should also include the impact of specific treatments of BCC on HRQoL, since these data are essential as well to help balancing the risk for both over- and undertreatment. The burden of treatment obviously differs per individual patient and the treatment method used. Nevertheless, harms caused by BCC treatment are common, although mostly mild to moderate.[39-41] Examples of these treatment related harms are direct side effects of treatment (e.g. bleeding, infection, pain, poor wound healing, numbness or itching, motor function problem, local allergic reaction to bandages or antibiotics), but also indirect problems related to treatment (e.g. anxiety, depression, problems with scar or appearance). Furthermore, the (additional) burden of treatment in frail older adults may be significant due to factors such as functional impairment, the need for (repeated) hospital visits, travel distance, support needed by relatives etc.

Combining and implementing more evidence regarding the natural course and impact on HRQoL of BCC (treatment) in daily clinical practice, might stimulate a more holistic, patient-specific approach and thereby improve skin cancer care in frail older adults. These same principles could be used for the other subtypes of NMSC.

Balancing under- and overtreatment to a greater extent: the time to benefit principle, choosing management goals and the introduction of watchful waiting

"Time to benefit" is defined as the time between an intervention and the time when a significant improvement in health outcomes becomes evident. Previously, this term was mainly used and studied in preventive medicine, e.g. cancer screening or the prescription of statins.[42,43] The same principles used before might be applicable to skin cancer care, especially in patients with low-risk asymptomatic NMSC. Therefore, future studies on this concept are strongly recommended. Together with the previously mentioned data on general prognosis, natural tumor course and impact on health-related quality of life of tumor and treatment, balancing under- and overtreatment might become easier in daily practice.

In addition, it should be pointed out that different management goals can be chosen in skin cancer care (curation, prevention of functional impairment, relieving symptoms etc.). The management goal(s) should be carefully chosen together with the patient, his or her relatives when applicable, and the referring physician. Current healthcare systems and caregivers often tend to be preoccupied with curation. This may especially be a pitfall in the population of frail older adults, since treatment goals other than curation might be in the best interest of a patient. In this context, it is important to remember that most studies and guideline-recommendations focus on curation as outcome measure of interest, when using these for guidance in daily practice.

Furthermore, after gaining more time to benefit data, the decision not to treat a NMSC and to perform *watchful waiting* might become a better justifiable, evidence-based, and generally accepted option in some frail older adults. The option of watchful waiting might lead to further optimization of skin cancer care. More research designed to explore this option in skin cancer care is recommended. Previous cancer research already showed the added value of watchful waiting as an option in different types of cancer with a relatively low-malignant potential, e.g. some forms of prostate cancer and hematologic malignancies.[44,45]

It should be mentioned that balancing the risk for under- and overtreatment of NMSC might be influenced by financial incentives as well. Although general statements cannot be made, one cannot avoid the impression that a caregiver may be influenced by the financial compensation gained by performing treatment, while balancing management considerations. In other words, the (potential) existence of financial-driven treatment decisions should not be forgotten in a discussion on tailoring skin cancer management.

Frailty: conceptualization, determination, and implementation in skin cancer care

Although the exact conceptional and operational definitions of frailty are still under discussion, most experts consider frailty as a clinical state of vulnerability due to a declined functional reserve of multiple physiologic systems. Although frailty, aging and comorbidity are closely related terms, it is more and more believed frailty is a separate entity with its own pathofysiology. It is thought that a cumulative decline in functioning of several processes in the body, influenced by genetic, epigenetic and environmental factors related to aging, can result in disproportional health status changes due to minor stressor events after reaching a certain frailty threshold. Consequently, frailty results in an increased risk for poor health outcomes like falls, disability and death.[46]

As emphasized above, it might be of additional value to include frailty and its potential consequences as a separate entity in skin cancer management considerations as well.

Determination of frailty in daily dermatological practice might be a challenge. Comprehensive geriatric assessment is considered the gold standard for frailty detection and several derivative screening tools are available as well (e.g., Vulnerable Elders Survey-13, Geriatric 8, or Groningen Frailty Index).[47] However, current literature lacks any evidence on validation in skin cancer care and feasibility for usage in daily dermatological practice can be questioned in some of these tools due to their comprehensiveness. Development of a validated and feasible screening tool for dermatologic practice is recommended. Obviously, critical evaluation of the benefits of such a screening tool should be performed additionally.

Guidance from clinical practice guidelines in frail older adults with nonmelanoma skin cancer

In **Chapter 8** the applicability of CPGs on NMSC in older adults was studied. A broad desire was identified on integration of items related to frail older adults in NMSC CPGs, but after systematically reviewing current guidelines this integration was shown to be limited.

Consequently, several recommendations were made to improve the attention for frail older adults in CPGs. More attention for this population in CPGs might stimulate caregivers to further tailor and personalize their management decisions, together with the patient, family and other relevant caregivers. Including items in a CPG does not necessarily mean a behavioral change in caregivers daily practice, but might be of value as a first step. Nevertheless, other measurements are recommended which might increase the awareness for this subject and stimulate a behavioral change as well, e.g. generating more evidence-based guidance by additional studies on the subject (as mentioned before), and including more attention for management decisions in frail older adults in educational programs (e.g. the CanBetter-program, as discussed before).[30,48]

Furthermore, intensive collaboration with caregivers which are more experienced in management considerations in frail older adults (e.g. geriatricians, elderly care specialist) should be encouraged. Principles adapted in management considerations in frail older adults by these experienced caregivers might be applicable in skin cancer care. For example, the Dutch Association of Clinical Geriatrics and the The Dutch Society of Internal Medicine developed general recommendations to provide assistance in the development of "older adult-proof" CPGs, which can be very useful in the field of dermatology as well.[49]

A final consideration which should be pointed out is the role of CPGs in current clinical medicine. CPGs are more and more considered as standard of care and CPGs are increasingly used as quality indicators and performance incentives by several parties.

Therefore, flexibility for tailoring management or deviation from clinical standards in the context of a CPG is considered of significant importance.[48,50]

Final considerations regarding nonmelanoma skin cancer management in frail older adults

In conclusion, management of NMSC in frail older adults remains challenging. Key elements expected to provide guidance to clinicians in daily practice and to improve tailoring of skin cancer care in this population are: more research, better CPG-integration, and improving education and interdisciplinary collaboration on this topic.

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Summary and conclusions

Summary

Healthcare providers are expected to be increasingly confronted with the growing population of older adults. In the Netherlands, the frailest and most dependent older adults live in nursing homes. Skin problems are common in this patient population and they can result in a high level of morbidity, causing a significant impact on quality of life. Management decisions in frail older adults may be challenging since several factors should be taken in consideration, such as a limited life expectancy, immobility, and dementia. A major group of skin disorders resulting in these challenges in frail older adults is skin cancer. The most common subgroup of skin cancer is nonmelanoma skin cancer (NMSC), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) and its precursors. NMSC has a relative low-malignant natural course compared to many other types of cancer, however the impact on quality of life in the longer term may be significant. Balancing the risk of under- and overtreatment in older adults with NMSC, together with patient- and tumor characteristics is therefore not easily performed.

The aims of the studies presented in this thesis were to obtain insight in the current need for, provision of, and quality of general dermatologic care among nursing home patients (Part A of this thesis), and to study current skin cancer care among older adults and provide guidance in medical-decision making (Part B of this thesis).

Dermatologic care in institutionalized older adults

In **Chapters 2 and 3** two nationwide surveys are described aimed to assess the need for and provision of dermatologic care in Dutch nursing homes from both the perspective of physicians working in nursing homes and dermatologists.

Nursing home physicians (NHPs) are often confronted with skin problems among their patients (62.5% ≥10 times during the last 3 months), mostly (pressure) ulcers, eczema, and fungal infections. A lack of availability and experience of NHPs were noted to limit the possibility to diagnose and treat common skin problems in nursing home patients. Dermatology outpatient clinic visits or other forms of consultation of a dermatologist are frequently needed according to the responding NHPs, especially in case of (a suspicion of) a cutaneous (pre)malignancy. The vast majority of the NHPs indicated to collaborate with a dermatologist on a regular basis (79.3% ≥1 time(s)/year, 41.5% ≥4 times/year), mostly by phone. Moreover, 88.5% of the NHPs noted one or more of their patients visited a dermatology outpatient clinic during the last year. Almost all participating NHPs received some form of basic dermatology training (mostly during medical school). However, more

and better training was requested by a majority of the NHPs, especially regarding cutaneous (pre)malignancies.

Dermatologists and dermatology residents noted that 79.2% ever had contact with a NHP concerning a nursing home resident, mostly by phone. In contrast, only a minority (30.0%) ever visited a patient within a nursing home. Of these respondents, nursing homes are mostly visited on a regular basis (48.7% ≥4 times/year). A majority of the dermatologists and dermatology residents (68.5%) is willing to visit (more) patients within a nursing home, but a lack of time and inadequate financial compensation are mentioned as important barriers. Cutaneous (pre)malignancies (51.4%), eczema/dermatitis (25.7%) and (pressure) ulcers (8.6%) were mentioned as the most common reasons for dermatologists to visit a nursing home patient. Most dermatologists visiting patients within nursing homes perform diagnostic and treatment procedures within the nursing home, ranging from punch biopsy (65.7%) and dermatoscopic examination (62.9%), to cryotherapie (68.6%) and surgical excision (22.9%). Nevertheless, diagnostic and treatment procedures are less frequently used by dermatologists in a nursing home compared to the dermatology outpatient clinic. This less frequent use of procedures may reflect a deliberate omission in the best interest of a patient, for instance to prevent an unnecessary patient burden in case of a limited life expectancy. However, unavailability of a diagnostic of treatment procedure and a lack of supporting staff are other frequently mentioned reasons which could possible lead to an unintended omission of a contemplated procedure.

The respondents in the two nationwide surveys were additionally asked how they believe that dermatologic care among nursing home patients can be improved, as described in **Chapters 2 and 4** (for NHPs and dermatologists, respectively). The most frequently made suggestion in both groups was better utilization of telemedicine applications (21.6% and 26.5% of the suggestions made by NHPs and dermatologists, respectively). More nursing home visits by dermatologists was the second commonly made suggestion in both groups of physicians (21.4% and 22.1%, respectively). Other suggestions to improve dermatologic care among nursing home patients were: (1) better education of healthcare providers and (2) to improve the availability of diagnostic and/or treatment procedures needed to provide proper dermatologic care.

Skin cancer care in frail older adults

As described before, skin cancer is common among nursing home patients. Therefore, the current and potential future role of NHPs in skin cancer management was studied in more detail (**Chapter 5**). It was found that NHPs consider their knowledge to diagnose the different skin cancer subtypes to be sufficient, with the exception of Bowen's disease.

Though, only a minority of the NHPs considered their knowledge and experience to be sufficient to treat all different skin cancer subtypes. A minority of the respondents performed treatment of skin cancer or precursor lesion on their own initiative (37.8%) or after dermatologist consultation (57.6%). Actinic keratosis was the subtype treated the most by NHPs. Cryotherapy and topical 5-fluorouracil were the treatment options most often used by NHPs. Most of the NHPs (94.5%) expected to be able to perform treatment more frequently after more education. Most NHPs indicated that the role of dermatologists in the diagnosis and treatment of skin cancer remains essential, especially in SCC and melanoma.

In **Chapter 6**, a study is described which aimed to assess the influence of high age and comorbidity on the management of NMSC. Since these factors are closely related to a limited life expectancy, it was hypothesized these factors would influence management decisions and guideline-adherence. However, the results of this study showed NMSC management is not or only minimally influenced by high age and comorbidity, which was in contradiction with our expectations. Future research on general prognostication, prediction of the patient burden caused by tumor and treatment, and time to benefit in NMSC management is strongly recommended.

In **Chapter 7** current literature was systematically reviewed on the epidemiology and clinicopathological features of BCC in persons aged ≥80 years. BCC is the type of skin cancer with the lowest malignant potential. This often creates management dilemma's as mentioned before. It was found that the incidence rates of BCC among persons aged ≥80 years are high and increasing over time. Furthermore, BCC in this population are more prevalent in men, most often of the nodular subtype, and located in the head and neck area. Little is known regarding the impact on health-related quality of life of BCC and data concerning prognostication is scarce. These topics should be further studied in the future, to provide better guidance for clinicians in daily practice dilemma's.

More guideline-integration of items related to NMSC management in frail older adults might assist clinicians to determine the most appropriate skin cancer care in their individual patients. In **Chapter 8** a multidisciplinary working group was formed to collect and prioritize items related to frail older adults with NMSC for integration into clinical practice guidelines (CPGs). Additionally, a systematic review was performed to assess the current integration of these items in CPGs. It was found that CPG-integration of many items is broadly desired, but currently limited. Recommendations for future CPG-development were provided.

Conclusions

To conclude, this thesis provides insight in the current status of dermatologic care among frail older adults, especially those inhabiting nursing homes and those suffering from skin cancer. Important challenges and limitations in dermatologic care among frail older adults were found and suggestions to optimize dermatologic care in these populations were provided.

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Nederlandse samenvatting en conclusies

Nederlandse samenvatting

Naar verwachting zullen zorgverleners in de toekomst steeds vaker geconfronteerd worden met het groeiend aantal ouderen. In Nederland wonen de meest kwetsbare en afhankelijke ouderen in verpleeghuizen. Huidproblemen komen veel voor in deze patiëntpopulatie en kunnen veel klachten veroorzaken. Daardoor kunnen huidproblemen een aanzienlijke invloed hebben op de kwaliteit van leven. Behandelafwegingen bij kwetsbare ouderen kunnen een uitdaging zijn, aangezien verschillende factoren in overweging genomen dienen te worden. Voorbeelden van deze factoren zijn een beperkte resterende levensverwachting, immobiliteit en dementie. Huidkanker is een veelvoorkomend probleem bij kwetsbare ouderen, waarbij deze uitdagingen met betrekking tot behandelafwegingen duidelijk naar voren komen. De meest voorkomende subgroep van huidkanker wordt gevormd door niet-melanoom huidkanker, welke het basaalcelcarcinoom (BCC) en het plaveiselcelcarcinoom (PCC) met diens voorstadia omvat. Niet-melanoom huidkanker heeft een relatief laag-maligne natuurlijk beloop vergeleken met veel andere vormen van kanker. Desalniettemin kan de invloed van niet-melanoom huidkanker op de kwaliteit van leven op de langere termijn aanzienlijk zijn. Het afwegen van het risico op onder- en overbehandeling van niet-melanoom huidkanker bij ouderen en het meewegen van patiënt- en tumorkenmerken daarbij is daarom niet eenvoudig.

De doelstellingen van het onderzoek beschreven in dit proefschrift waren om meer inzicht te krijgen in de vraag naar, het aanbod van, en de kwaliteit van algemene dermatologische zorgverlening onder verpleeghuispatiënten (Deel A van dit proefschrift). Daarnaast werd de huidige huidkankerzorg voor ouderen bestudeerd en getracht ondersteuning te bieden bij behandelafwegingen (Deel B van dit proefschrift).

DERMATOLOGISCHE ZORG VOOR VERPLEEGHUISPATIËNTEN

In **Hoofdstuk 2 en 3** worden twee landelijke vragenlijstonderzoeken beschreven over de vraag naar en het aanbod van algemene dermatologische zorg in Nederlandse verpleeghuizen, vanuit het perspectief van artsen werkzaam in verpleeghuizen en dermatologen.

Artsen werkzaam in verpleeghuizen worden vaak geconfronteerd met huidproblemen bij hun patiënten (62.5% ≥10 keer gedurende de afgelopen 3 maanden), met name wonden (inclusief decubitus), eczeem en schimmelinfecties. Een beperkte beschikbaarheid van diagnostische en therapeutische hulpmiddelen, alsmede een beperkte ervaring hiermee, werd door deze artsen benoemd als belangrijke limitaties om zelf de optimale dermatologische zorg te kunnen leveren aan hun patiënten. De overgrote meerderheid van

de artsen werkzaam in verpleeghuizen consulteert regelmatig een dermatoloog op afstand (79.3% ≥1 keer/jaar, 41.5% ≥4 keer/jaar), meestal telefonisch. De belangrijkste reden voor deze consultaties is (de verdenking op) huidkanker of een voorstadium hiervan. Daarnaast geeft 88.5% van alle artsen werkzaam in verpleeghuizen aan dat één of meer van hun patiënten een polikliniek dermatologie bezocht gedurende het afgelopen jaar. Vrijwel alle participerende artsen werkzaam in verpleeghuizen volgden in het verleden basaal dermatologisch onderwijs (meestal gedurende de basisopleiding geneeskunde). Desalniettemin gaf het merendeel van de artsen aan meer en beter dermatologisch onderwijs te willen, met name op het gebied van huidkanker.

Dermatologen (in opleiding) gaven aan dat 79.2% van hen ooit contact had met een arts uit een verpleeghuis over een verpleeghuispatiënt, meestal telefonisch. Slechts een minderheid van hen (30.0%) bezocht ooit een patiënt op locatie binnen een verpleeghuis. De respondenten die wel eens patiënten op locatie binnen het verpleeghuis bezoeken doen dit meestal op regelmatige basis (48.7% ≥4 keer/jaar). Een meerderheid van de dermatologen (in opleiding) is bereid om (meer) patiënten binnen een verpleeghuis te bezoeken voor beoordeling, maar een gebrek aan tijd en ontoereikende financiële compensatie worden genoemd als belangrijke drempels. Huidkanker en voorstadia (51.4%), eczeem (25.7%) en wonden (inclusief decubitus) worden aangegeven als de meest voorkomende redenen voor dermatologen om patiënten op locatie binnen een verpleeghuis te bezoeken. De meeste dermatologen die patiënten bezoeken binnen een verpleeghuis verrichten aldaar ook diagnostische en therapeutische verrichtingen, variërend van het nemen van een stansbiopt (65.7%) en dermatoscopische beoordeling (62.9%), tot cryotherapie (68.6%) en chirurgische excisie (22.9%). Desalniettemin worden er minder diagnostische en therapeutische verrichtingen uitgevoerd door dermatologen binnen het verpleeghuis in vergelijking met de polikliniek. Enerzijds zou dit kunnen wijzen op het weloverwogen en gewenst afzien van bepaalde diagnostiek of therapie in het algemeen belang van de patiënt, bijvoorbeeld om onnodige belasting voor de patiënt te voorkomen bij een beperkte levensverwachting. Echter, het onvoldoende beschikbaar zijn van benodigde materialen en ondersteunend personeel worden ook frequent genoemd als redenen voor het genoemde verschil tussen het verpleeghuis en de polikliniek. Dit kan leiden tot het ongewenst moeten afzien van een voorgenomen diagnostische en/of therapeutische verrichting.

De respondenten in de twee landelijke vragenlijstonderzoeken werden vervolgens gevraagd hoe zij denken dat de dermatologische zorg voor verpleeghuispatiënten verbeterd zou kunnen worden, zoals beschreven in **Hoofdstuk 2 en 4** (respectievelijk voor artsen werkzaam in verpleeghuizen en dermatologen). Het meest genoemde verbeterpunt door beide groepen artsen was het beter gebruik maken van teledermatologie (21.6% en 26.5%

van de genoemde verbeterpunten door artsen werkzaam in verpleeghuizen en dermatologen respectievelijk). Meer verpleeghuisbezoeken door dermatologen werd tevens vaak genoemd als verbeterpunt door beide groepen artsen (21.4% en 22.1%). Andere belangrijke suggesties die werden gedaan zijn: (1) betere scholing van zorgverleners en (2) verbetering van de beschikbaarheid van benodigdheden voor diagnostiek en therapie.

Huidkankerzorg voor kwetsbare ouderen

Zoals eerder beschreven komt huidkanker veel voor bij verpleeghuispatiënten. Daarom werd de huidige en mogelijke toekomstige rol van artsen werkzaam in verpleeghuizen in de huidkankerzorg in meer detail bestudeerd (**Hoofdstuk 5**). Er werd gevonden dat artsen werkzaam in verpleeghuizen hun kennis over de verschillende subtypen huidkanker als voldoende beschouwen om ze te kunnen herkennen, met uitzondering van morbus Bowen (een voorstadium van het PCC). Desalniettemin beschouwt slechts een minderheid van de respondenten hun kennis en ervaring als voldoende om behandeling uit te voeren. Slechts een beperkt deel van de artsen werkzaam in verpleeghuizen behandelde eerder een vorm van huidkanker of voorstadium op eigen initiatief (37.8%) of na consultatie van een dermatoloog (57.6%). Het meest behandelde subtype door de respondenten was actinische keratose (een voorstadium van het PCC). Cryotherapie en 5-fluorouracil crème waren de meest toegepaste behandelmethoden door artsen werkzaam in verpleeghuizen. De meeste respondenten (94.5%) gaven de verwachting aan vaker behandeling te kunnen verrichten na meer scholing. Daarentegen gaf de meerderheid van de artsen ook aan dat zij de rol van de dermatoloog bij de diagnostiek en therapie van huidkanker essentieel vinden, met name in het geval van een PCC of melanoom.

In **Hoofdstuk 6** is de invloed van hoge leeftijd en comorbiditeiten op de beleidsbepaling bij niet-melanoom huidkanker onderzocht. Aangezien deze factoren een sterke samenhang hebben met resterende levensverwachting werd verwacht dat zij van invloed zouden zijn op beleidsbepaling en richtlijnadherentie (het wel of niet opvolgen van aanbevelingen uit richtlijnen). Echter, de resultaten van de studie tonen dat het beleid bij niet-melanoom huidkanker niet of nauwelijks wordt beïnvloedt door hoge leeftijd en comorbiditeiten. Toekomstig onderzoek naar het bepalen van de algehele prognose van een patiënt, het voorspellen van de belasting voor de patiënt door de tumor en eventuele behandeling, en de tijd nodig om de voordelen van behandeling op te laten wegen tegen de eventuele nadelen van behandeling (*Engels: time to benefit*) worden sterk aanbevolen.

In **Hoofdstuk 7** werd de huidige literatuur systematisch bestudeerd naar beschikbare informatie over de epidemiologie en de clinicopathologische karakteristieken van BCC bij personen van 80 jaar en ouder. BCC is de meest voorkomend vorm van huidkanker, met

tegelijkertijd het minst maligne karakter van alle huidkankervormen. Zoals eerder beschreven resulteert dit vaak in behandeldilemma's. Vanuit de huidige beschikbare literatuur werd gevonden dat de incidentiecijfers van BCC bij personen van 80 jaar en ouder hoog zijn en toenemen door de tijd. Daarnaast komt BCC in deze leeftijdscategorie vaker voor bij mannen, betreft het meestal het nodulaire subtype en bevindt het BCC zich meestal in het hoofdhalsgebied. Er is weinig bekend over de impact van BCC op de gezondheidsgerelateerde kwaliteit van leven van een patiënt en gegevens over prognosticering zijn tevens schaars. In de toekomst zouden deze aspecten beter onderzocht moeten worden om zorgverleners beter te kunnen ondersteunen bij behandeldilemma's in de dagelijkse praktijk.

Meer richtlijnintegratie van aspecten gerelateerd aan beleidsbepaling bij niet-melanoom huidkanker bij kwetsbare ouderen zou zorgverleners mogelijk kunnen helpen bij behandeldilemma's in de dagelijkse praktijk. In **Hoofdstuk 8** werd door een multidisciplinaire werkgroep een lijst samengesteld met aspecten gerelateerd aan niet-melanoom huidkanker bij kwetsbare ouderen. Vervolgens werden deze aspecten geprioriteerd op basis van de wens om hieraan meer aandacht te schenken in richtlijnen over niet-melanoom huidkanker. Tot slot werden de huidige richtlijnen systematisch beoordeeld op de integratie van deze aspecten. Er werd gevonden dat er verschillende aspecten zijn waarbij de wens tot meer richtlijnintegratie groot is, maar dat de huidige richtlijnintegratie slechts beperkt is. Aanbevelingen worden daarom gedaan voor richtlijnontwikkeling in de toekomst.

Conclusies

Concluderend biedt dit proefschrift inzichten in de huidige staat van dermatologische zorgverlening aan kwetsbare ouderen, in het bijzonder verpleeghuispatiënten en oudere patiënten met huidkanker. Een aantal belangrijke uitdagingen en limitaties in de dermatologische zorgverlening onder kwetsbare ouderen werden gevonden en aansluitend werden suggesties gedaan om de zorg in deze patiëntpopulatie te verbeteren.

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List of publications
Curriculum vitae
Dankwoord (acknowledgements)
List of abbreviations

List of publications

Publications related to this thesis

Lubeek SF, van der Geer ER, van Gelder MM, Koopmans RT, van de Kerkhof PC, Gerritsen MJ. Current dermatologic care in Dutch nursing homes and possible improvements: a nationwide survey. *J Am Med Dir Assoc.* 2015; 16(8): 714.e1-6. doi: 10.1016/j.jamda.2015.04.015.

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Curriculum vitae

Satish Frank Kishore Lubeek werd geboren op 18-10-1987 in Nijmegen. Nadat hij in 2005 aan de Nijmeegse Scholengemeenschap Groenewoud zijn Gymnasium diploma cum laude behaalde begon hij aan de studie Geneeskunde aan de Universiteit Utrecht. In verband met zijn groeiende nevenactiviteiten op de stijldansvloer werd Utrecht na twee jaar verruild voor Nijmegen, alwaar hij in 2012 zijn studie cum laude afrondde.

Tijdens zijn studie ontwikkelde Satish een bijzondere interesse voor zowel de geneeskundige zorg voor kwetsbare ouderen als de dermatologie, waarna diverse keuzecoschappen en onderzoeksactiviteiten volgden. Na enkele maanden als basisarts in de verpleeghuiszorg te hebben gewerkt kon Satish in 2012 starten op de afdeling Dermatologie van het Radboudumc. Aanvankelijk heeft hij gedurende zes maanden als ANIOS (artsassistent niet in opleiding tot specialist) gewerkt en per januari 2013 kon aangevangen worden met de specialistenopleiding tot dermatoloog. Tegelijkertijd besloot Satish onderzoek te starten naar de dermatologische zorg voor kwetsbare ouderen, dat gaandeweg werd uitgebouwd tot het proefschrift dat voor u ligt.

Naast zijn opleiding en onderzoeksactiviteiten houdt Satish zich ook met veel plezier bezig met het ontwikkelen en verzorgen van onderwijs omtrent geriatrische dermatologie aan diverse doelgroepen en participeert hij in verschillende regionale en landelijke werkgroepen op het gebied van kwetsbare ouderen, geriatrische dermatologie en behandelbeperkingen. In 2015 werd een subsidie verworven voor nader onderzoek op het gebied van teledermatologische consultatie binnen de verpleeghuissetting, wat in 2016 opgestart werd. In 2016 had Satish de eer om de Jonge Leeuw dermatologieprijs in ontvangst te mogen nemen voor zijn werkzaamheden rondom de zorg voor kwetsbare ouderen.

In de toekomst hoopt hij zich bezig te kunnen blijven houden met het verbeteren van de dermatologische zorg voor kwetsbare ouderen. Satish woont al jaren gelukkig samen met Joris van Loveren in Nijmegen.

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List of abbreviations

5FU	topical 5-fluorouracil
95%CI:	95% confidence interval
ACN	Australian Cancer Network
AGREE II	Appraisal of Guidelines for Research and Evaluation II instrument
AJCC	American Joint Committee on Cancer
ANAES	French National Agency for Accreditation and Evaluation in Healthcare *(French: Agence Nationale d'Accréditation et d'Évaluation en Santé)*
APC	annual percentage change
AK	actinic keratosis
BAD	British Association of Dermatologists
BD	Bowen's disease
BCC	basal cell carcinoma
CCA	Cancer Council Australia
CCI	Charlson comorbidity index
CME	continuing medical education
CPG	clinical practice guideline
CRYO	cryotherapy
DDG	German Society of Dermatology *(German: Deutschen Dermatologischen Gesellschaft)*
DKG	German Cancer Society *(German: Deutsche Krebsgesellschaft)*
DLQI	Dermatology Life Quality Index
DOC	dermatology outpatient clinic
EADO	European Association of Dermato-Oncology
EDF	European Dermatology Forum
EMBASE	Excerpta Medica Database
EORTC	European Organization for Research and Treatment of Cancer
FACT-G	Functional Assessment of Cancer Therapy-General
G8	Geriatric 8
GA	geriatric assessment
GFI	Groningen Frailty Index
HRQoL	health-related quality of life
i/morfBCC	infiltrative/morpheaform basal cell carcinoma
IMI	topical imiquimod
IR	incidence rate
LE	life expectancy
mBCC	metastatic basal cell carcinoma
MeSH	Medical Subject Headings
MMS	Mohs micrographic surgery
MR	mortality rate
NA	not applicable
nBCC	nodular basal cell carcinoma
NCCN	National Comprehensive Cancer Network
NHP	nursing home physician
NMSC	nonmelanoma skin cancer
NR	not reported

NVDV	Dutch Dermatological and Venereological Society *(Dutch: Nederlandse Vereniging voor Dermatologie en Venereologie)*
OR	Odds ratio
PALGA	Dutch national pathology database *(Dutch: Pathologisch Anatomisch Landelijk Geautomatiseerd Archief)*
PDT	photodynamic therapy
PHI	permanent healthcare institution
Pinkus	fibroepithelioma of Pinkus
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoE	quality of evidence
QRS	quality rating scheme
RT	radiotherapy
SAMPL	Statistical Analyses and Methods in the Published Literature
sBCC	superficial basal cell carcinoma
SCC	squamous cell carcinoma
SD	standard deviation
SE	surgical excision
S&F	store-and-forward
SF-36	36-Item Short Form Health Survey
SFD	French Dermatology Society *(French: Société Française de Dermatologie)*
SIGN	Scottish Intercollegiate Guidelines Network
SPSS	Statistical Package for Social Sciences
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
SUR	surgery
UVR	ultraviolet radiation
VES-13	Vulnerable Elders Survey-13
YoE	years of experience